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EDWARD B. D. NEUHAUSER

Caldwell Lecturer, 1952

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GROWTH, DIFFERENTIATION, AND DISEASE

CALDWELL LECTURE, 1952*

By EDWARD B. D. NEUHAUSER, M.D.

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BOSTON, MASSACHUSETTS

I WOULD like to thank Doctor Bromer for his generous introduction and Doctor Martin, President of The American Roentgen Ray Society for the honor of being asked to deliver this lecture tonight at the first Annual Meeting of the Society in the State of Texas. I am equally aware of the responsibility that this lecture entails because tonight we pay tribute to one of the great pioneers of Radiology, Dr. Eugene Caldwell. There must be few remaining radiologists who knew Doctor Caldwell intimately; I, myself, was born the year he was President of this Society, yet we are all heirs of his accomplishments and intellectual endeavors. He was an electrical engineer and radiologist whose contributions were many. For one who loves the New England Coast there is a fascination in Caldwell's attempt, early in his career, to lay a submarine telephone cable to Pollock Rip Lightship. For those who are interested in the physical equipment of a radiologist his numerous useful inventions are remarkable. His contributions to the medical literature were many, but perhaps most important of all he did, in the words of Percy Brown,[3] "elevate Radiology from a quasi-photographic pastime with low commercial overtones to the medical science that it is today."

The subject of tonight's talk "Growth, Differentiation, and Disease" will certainly need clarification. Wetzel[16] has defined growth as "that fundamental property of living things concerned only with their change in size or number, as distinguished from the co-relative property of differentiation which has to do with changes in kind or type of structure. Acting together growth and differentiation result in the development of an organism." The foregoing definition expresses an important concept so tersely that perhaps further amplification will make it clear. It means that growth is an increase in the size of the whole or a part of a living organism or an increase in the number of the cellular components that make up the part. On the other hand, differentiation implies a change of the components of the part into some-

* Delivered at the Fifty-third Annual Meeting of the American Roentgen Ray Society, Houston, Texas, September 23–26, 1952.

thing else. The orderly sequences of growth and differentiation together will lead to normal development.

Pediatric Radiology is in great part the study of the interaction of this development and disease and the alteration of the normal pattern produced by the impact of the various stresses of the environment in which the organism must live.

I would like to present to you tonight a series of exhibits which I hope will demonstrate this interaction. Let us commence at the borderline of genetics and embryology around which we must tread cautiously. It has been said that there are two factors responsible for development, genetic and environmental, but that these two cannot be completely separated will become clear.

Many diseases, presumably due to an abnormality in a single gene locus, are well known to us. Achondroplasia, marble bones, simple hereditary defects and many others can be attributed to a genetic abnormality. Gene mutation may likewise be responsible for a number of distinct abnormalities. It has been postulated[8] that once in ten thousand births there is a gene mutation that will produce achondroplasia which in turn will be expressed in subsequent offspring as a Mendelian dominant.

The environmental factors which may alter growth and development are very much more varied and more complicated. Of these, nutrition, abnormalities of the internal milieu, hormones, and the external environment of the organism, both prenatal and post-natal, are the most important.

It is now well known that genetic abnormalities may be entirely suppressed or be altered by environmental factors. Thus, in certain strains of white rabbits it is quite possible to pluck the white fur and then have it grown in black by subjecting the rabbit to a low temperature during the period of fur regrowth. Likewise, environmental abnormalities may react on the development of the organism in such a way that genetic abnormalities are simulated and the two may be indistinguishable clinically. Some of the agents responsible for these abnormalities are known. Infection of the pregnant woman with rubella will produce an abnormality that can be embryologically dated. Vitamin deficiencies, poorly understood abnormalities of diet whether protein or mineral, exposure to roentgen radiation, and many other noxious agents, such as nitrogen mustard, may produce lesions similar to those with a genetic basis.

The variety of skeletal and soft tissue malformations that presumably arise on a genetic background are legion and most are well known to the radiologist. However, the vast majority of malformations fall into general patterns, particularly those of the extremities associated with hypo- or hypersegmentation, and many malformations appear to be due to extreme hypoplasia or aplasia of a portion of the organism.

Of more particular interest are those abnormalities which arise from an aberration of tissue differentiation. Extreme hyperplasia, or local gigantism, is initiated during the first few months of fetal life. It represents, not an acceleration of growth, but a defect in the origin of the primordial part itself. Cessation of differentiation at some time during the process of limb bud development leads to "intra-uterine amputation," or may result in an annular zone of defective tissue. These zones appear at birth as deep circular scars and may be so deep as to interrupt the circulation, so that the survival of the limb distal to the scar is no longer possible.

A lesser defect may result only in a crease. This dysplasia of soft tissues so well described by Streeter[14] seems to develop as a localized cessation of differentiation during the first three or four months of fetal life. The extremity to be so involved shows sharply circumscribed areas of necrosis and degeneration of tissue that are replaced by scar. There is no evidence to suggest that such intra-uterine amputation or circular scarring is due to amniotic

Fig. 1. Cessation of differentiation has produced annular scars and defective development of the phalanges (Streeter's dysplasia).

bands or adhesions (Fig. 1).

Many of the neoplasms of infancy and childhood are congenital in nature and appear to arise as an abnormality of differentiation from groups of primordial cells that are pluri- or toti-potential and are capable of producing two or three germ layers. One, therefore, would expect to find a prevalence of tumors arising at those sites where cellular differentiation is most active. The sacrococcygeal teratoma is one of the most frequently seen tumors of the newborn infant. The accepted theory of origin is that this tumor arises from those undifferentiated but toti-potential cells that make up Hensen's node or "primitive knot."[5] As Hensen's node migrates toward the most caudal portion of the body those cells which will later form the "genital cells" are given off and these migrate anteriorly and are concentrated in the urogenital ridge. Abnormalities of differentiation of these cells will lead to teratomas anterior to the sacrum.

Neuroblastoma also arises as an abnormality of differentiation of tissue. This tumor may develop in a single focus or as multiple foci. However, differentiation may continue to alter the growth character of the tumor. A highly malignant neuroblastoma may mature into a relatively benign ganglioneuroma by continued cellular differentiation. It is entirely possible that the multiple foci of neuroblastoma so frequently found in the liver represents a multicentric origin of tumor in those collections of cells in the liver resembling neuroblasts and must not necessarily be interpreted as metastatic invasion. These few examples only suggest the multiplicity

of lesions and abnormalities that may arise through the process of differentiation.

Turning to normal growth and development we find it, too, dependent on many factors. It is naturally associated with proper hormonal balance because from imbalance abnormalities arise. Although in many instances the initiating abnormality of hormone influence is known and the clinical end picture has been recognized, many of the intermediary stages are poorly understood. Perhaps in our limited time tonight we should dismiss the subject by reminding you of the very large female in one of the lesser productions of Noel Coward who sings—"no one understands the inscrutable glands of a big girl like me."

Not only must there be adequate hormonal output in proper balance, but there must be ability of those end organs on which the hormones act to respond. Pseudohypoparathyroidism, a "Seabright bantam syndrome" where there is adequate hormone production, but an apparent inability of the end organs to respond to it, is characterized by a typical habitus. Patients with this abnormality are short, fat with round faces, and show brachydactyly. The shortening of the metacarpals is most pronounced in the first, fifth and fourth which are late in developing enchondral bone and are slow in forming secondary centers of ossification. Occasionally paraarticular calcification and calcification of the basal ganglia will be present.[1] One must not assume that all of these changes are due to a deficiency of the end organ response, but rather they may represent a greater abnormality of development. Whether this is on a genetic basis or whether it is due to postconception and environmental factors is not evident.

Just as the mechanism of hormonal action may not always be clear, so the effects of many of the known vitamins on the developing organism are still incompletely understood. Although many abnormalities that can be attributed either to excessive vitamin intake or to an inadequate vitamin intake are now known, probably all of the effects have not yet been recognized clinically. Both acute and chronic forms of vitamin A intoxication have been reported and the characteristic bone changes associated with chronic hypervitaminosis A are roentgenographically demonstrable. The work of Wolbach[17] and others suggests that this may not be the only osseous lesion that some day we should be able to identify. In laboratory animals prolonged feeding with excessive vitamin A produces changes that have not been recognized in the human. Elongation and overtubulation of the long bones is to be expected with an early excessive rate of enchondral bone formation, resulting in premature closure of the epiphyses. A diet that is deficient in vitamin A will produce in laboratory animals shortening of the long bones with delay in enchondral bone formation and marked inhibition of tubulation, but with apparent normal progression of appositional bone formation. The multiple fractures occurring in polar bears and other animals have been ascribed by the group at the Norsk Polarin Institutt[11] to excessive vitamin A intake.

One example of an abnormality of what Claude Bernard called the internal milieu is sufficient to indicate that normal function and normal metabolism of all the organ systems are essential for proper development. Hepatic rickets occurs in the newborn infant in the presence of severe liver disease or biliary obstruction and appears roentgenologically as a simple ordinary rickets. Although the osseous changes can be identified, it is by no means clear that the rachitic changes arise simply from failure of absorption or utilization of vitamins in the absence of bile, or whether it occurs, as has been suggested, because of a deficiency of some unidentified liver fraction.

But let us turn from the complexities of the internal environment to the wide and untouched field of roentgen investigation presented by the external environmental factors that may alter growth. Certain malformations due to faulty intra-uterine position

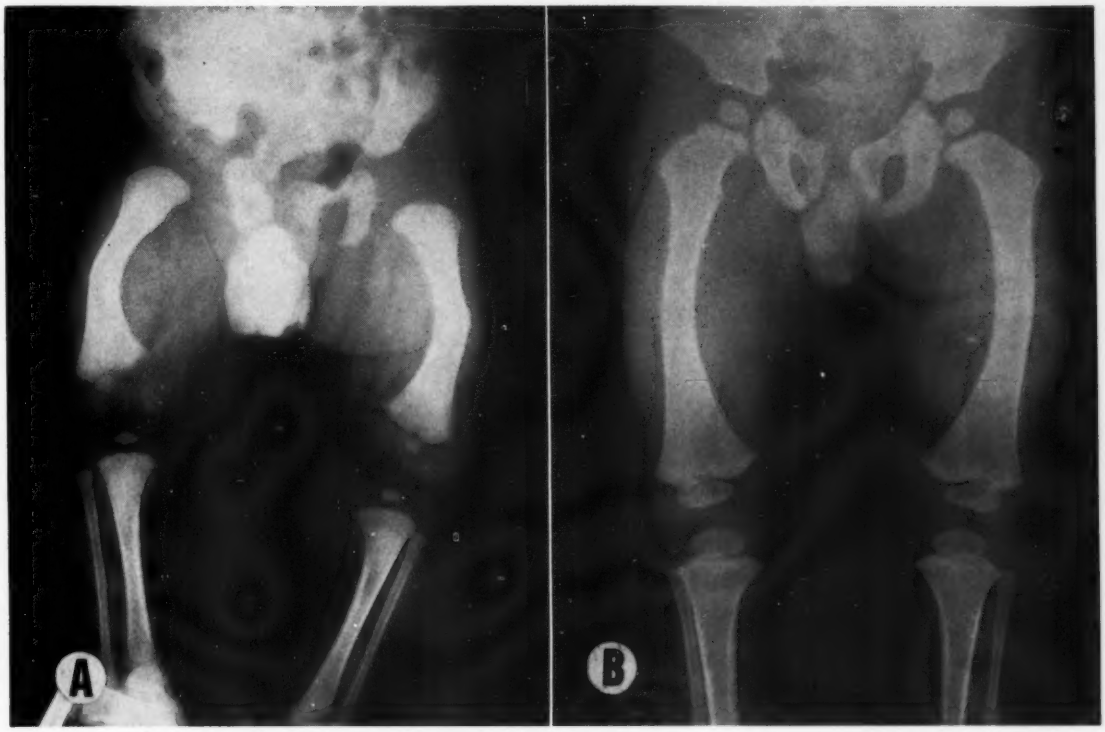


Fig. 2. (*A*) Bowing of each femur with soft tissue dimpling presumably produced by faulty intra-uterine position. (*B*) Same patient two years later. Although the deformity is less marked development alone may not be sufficient to correct a deformity in the diaphysis.

can be quite easily identified. Infantile bowing of the legs with skin dimpling may result from intra-uterine pressure of the opposite foot upon the mid portion of the thigh (Fig. 2, *A* and *B*). Other abnormalities, such as skull indentations from the pressure of a hand or foot during weeks or months of intra-uterine life have been recognized.[4] It is quite simple to identify the abnormal posture by placing the newborn infant in the position of comfort; bizarre positions of the limbs may result. A number of faulty postural habits established before birth may persist. Perhaps the most frequently seen is persistent adduction of one femur with contraction of the adductor muscles, elevation of the pelvis on the same side and an opposite lumbar scoliosis. Here an abnormality of growth continues. Faulty stress applied through the adducted femur to the acetabulum results in underdevelopment of the acetabulum with obliquity of the roof. It has been thought by many that this represents a primary acetabular dysplasia,[6] and such an entity may exist, but if the adduction contracture is corrected and proper stress applied to the acetabulum the dysgenesis promptly disappears and the acetabulum becomes essentially normal. The importance of the late effects in the adult of this rather simple abnormality is suggested by the statement of Putti[9] that 40 per cent of patients with coxae malum senilis developed degenerative arthritis because of stress applied for many years to a hip deformed by faulty posture or dysgenesis.

Once an abnormality of development has been initiated or created by one of the many factors that have been enumerated, it is possible by roentgen examination to study the interaction of growth in relation to that abnormality. Study of the growth of the skull in the presence of abnormality is rewarding. The weight of the brain of the newborn infant averages about 350 grams.

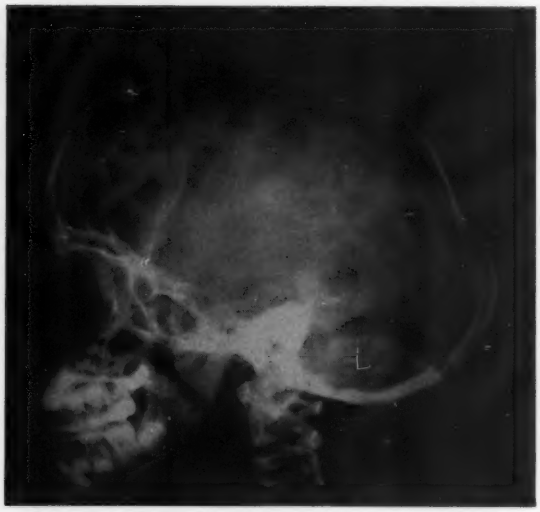


Fig. 3. Craniosynostosis. The lambdoidal suture alone is open. Skull contour and prominent digital markings suggest that normal brain development is present.

During the first year of life the brain increases almost threefold and has completed nearly half of its postnatal growth. By the end of the seventh year nine-tenths of the postnatal growth has been completed.[15] Not all portions of the brain grow at the same rate. The brain stem which is relatively large at birth undergoes diminution in proportionate size until the end of the first year, while the cerebellum shows a considerable increase in weight. The growth of the calvarium and base of the skull is dependent upon the growth of the brain, so that it is probable that some of the apparent abnormalities of the skull of the newborn infant are merely a reflection of the rate of the growth of the different portions of the brain. Thus, in the newborn the frontal portion of the skull appears quite underdeveloped and in an older child would certainly suggest a deficiency of the frontal portion of the brain. With experience one is able to recognize roentgenographically whether the osseous response to brain development is proceeding at a normal rate, or whether it is accelerated or diminished. This can be judged by contour, thickness of the bones and sutural prominence; and in many instances it is quite easy to suggest that there is a deficiency of cerebral development by an observation that the bones are thicker and the sutures less prominent than they should be. Microcephaly is, of course, an extreme example of this. If the deficiency of cerebral development is sufficiently marked there will be premature closure of the sutures and fontanelles, but this must be distinguished from a primary craniosynostosis.

Fig. 4. Sagittal synostosis without scaphocephaly. This mentally retarded child's cerebral development is insufficient to produce an abnormal skull contour.

We have never observed the onset of a craniosynostosis after birth. When all of the sutures are closed at birth the head is small with prominent digital impressions from increased intracranial pressure. If only one or a few sutures are closed a distinctive contour of the skull results (Fig. 3). The skull will expand predominantly parallel to the long axis of the closed suture. Scaphocephaly is produced by premature closure of the sagittal suture and a high vault by closure of the coronal suture. These changes in skull contour are not acquired by any characteristic of bone growth itself, but rather are due to the continued growth of the normal brain expanding and enlarging in the only direction that it can. However, if synostosis is associated with a sufficiently marked diminution in the rate of cerebral development no specific contour abnormality results. As can be seen in Figure 4, scaphocephaly is not present even though the sagittal suture is firmly closed.

Fig. 5. Hydrocephalus produced by a defective development "forking" of the aqueduct. The location of the obstruction can be suggested by the skull contour.

In the presence of obstructive hydrocephalus the contour of the skull depends on the site of obstruction, and frequently the site can be identified by the skull contour. In the presence of an aqueduct of

Fig. 6. Congenital obstruction of the foramina of Luschka and Magendie. The grossly enlarged fourth ventricle has herniated through the foramen magna.

Fig. 7. Congenital obstruction below the fourth ventricle. The posterior fossa is moderately enlarged and the lateral sinuses are high in position.

Fig. 8. Deeply serrated sutures without separation. The skull is enlarged and intracranial pressure increased. Osseous development has been accelerated by moderate hydrocephalus.

Silvius obstruction the posterior fossa is small, the tentorium displaced downward and the impressions on the bone produced by the lateral sinuses will be low in the occipital region (Fig. 5). If the obstruction is at the outlet of the fourth ventricle an entirely different picture may be seen. A congenital obstruction of the foramina of Luschka and Magendie will produce gross enlargement of the fourth ventricle in addition to dilatation of the lateral and third ventricles (Fig. 6). In this form of hydrocephalus the posterior fossa is relatively large, the lambdoidal sutures appear high in position and descent of the lateral sinuses from their fetal position in the low parietal region to the occipital region will have been prevented (Fig. 7).

In all forms of hydrocephalus the appearance of the skull sutures is dependent on the degree and duration of increased intracranial pressure. Although one usually expects to see separated sutures it is quite possible to have an intracranial pressure so slowly progressive that growth of the bones is able to maintain an adequate rate so that is no separation, but the serrations of the sutures may be unduly elongated (Fig. 9). Occasionally one will observe a patient with an obvious mental deficiency, in whom cerebral development cannot be

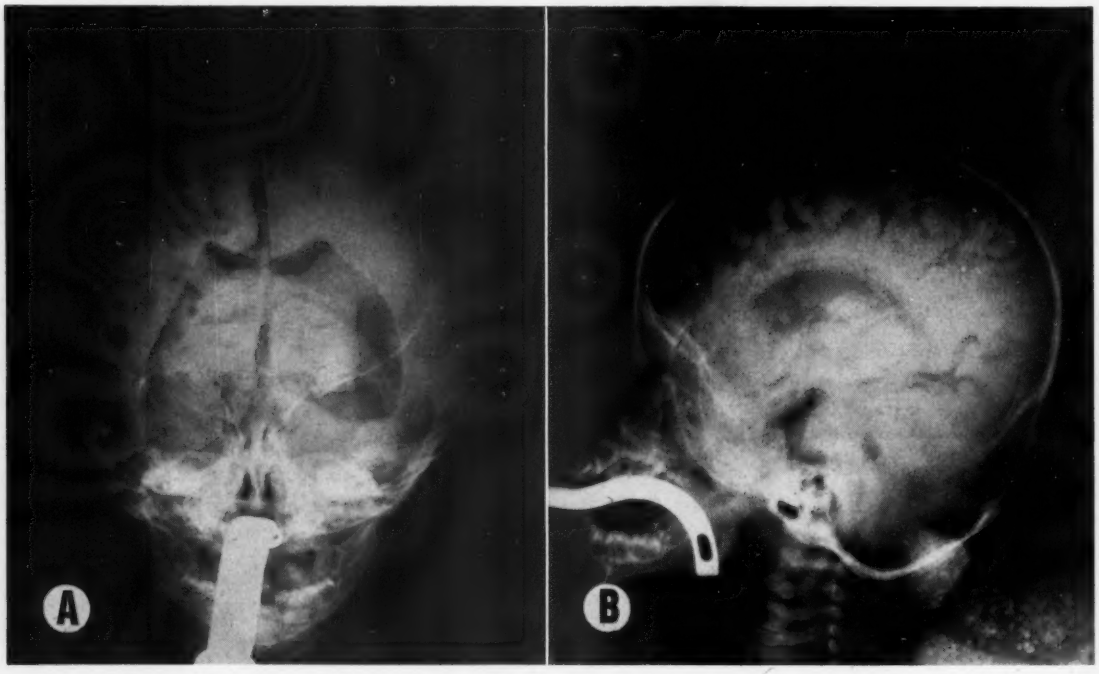


Fig. 9, (*A*) and (*B*) Deformity of the skull with enlargement of the middle fossa and bulging of the temporoparietal region associated with absence of the underlying dura.

continuing at a normal rate, where the skull size is not unusual. In these patients the pressure exerted by excessive cerebrospinal fluid is similar to that exerted by the development of the brain in the average individual, so that the skull enlarges at an essentially normal rate.

It is then evident that if the sutures and fontanelles are normal the skull produces a protective but not a restraining influence on the brain. Restraint, however, does appear to be exerted by the dura in controlling the pulsation of the brain. Osseous defects associated with an intact dura show no evidence of erosion, but in the presence of a deficient dura rapid erosion of the margin of a defect occurs. If there is no osseous defect, thinning of bone and localized prominence of the skull will take place over an area of dural deficiency (Fig. 9, *A* and *B*).

A number of simple abnormalities of growth can be studied roentgenographically during the development of the long bones. Many syndromes and lesions radiolucent due to lack of bone substance develop as abnormalities of conversion of cartilage into bone. Many cyst-like lesions appear in the metaphyseal zone, but these must be distinguished from cortical defects which unless viewed in profile resemble cysts. The fate of these small lesions

Fig. 10. "Simple bone cyst." The lesion involves the metaphysis and is of the same width as the meta physis. There is deficient tubulation.

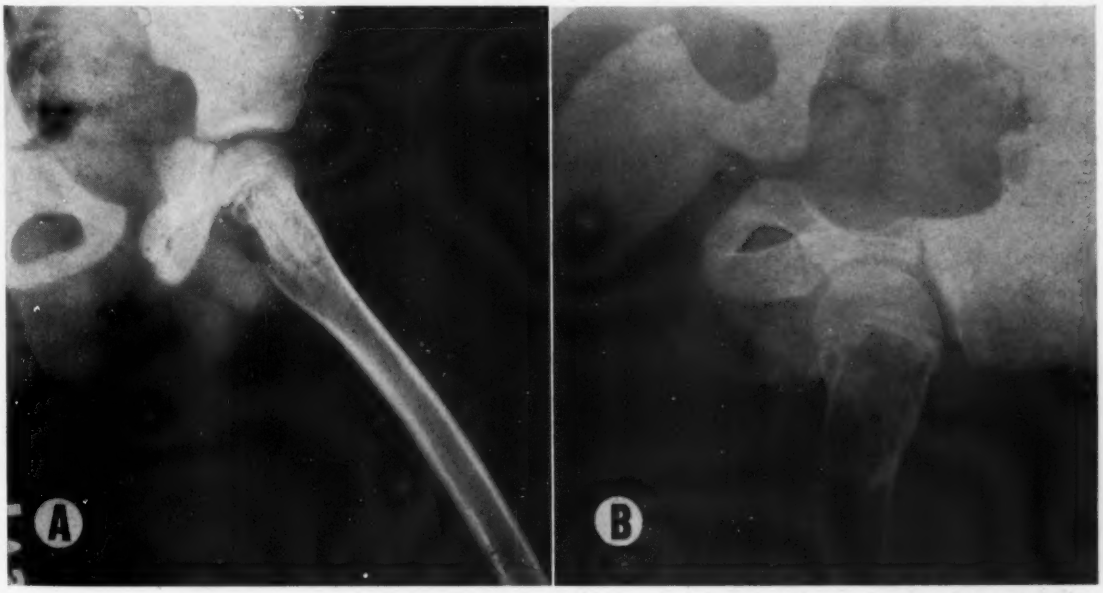


Fig. 11. (*A*) "Simple bone cyst" after curettage and filling with bone chips. The lesion involved the metaphysis. (*B*) The bone chips have been resorbed and the cyst is again evident. This would not have happened if submetaphyseal bone of normal architecture had been present.

Fig. 12. (*A*) This fracture occurred through that portion of the diaphysis where tubulation is active. (*B*) Restitution to normal after three years from longitudinal stress without torsion.

of faulty enchondral bone formation is variable. They may disappear entirely if centrally located as they can no longer be identified by roentgen means when present in the marrow cavity. If they lie at the periphery of the metaphysis they may disappear during the normal process of tubulation of the bone and may for a time be represented by a small area of nonresorption exostosis. It is possible that some of the cortical defects arise as a nonosseous conversion defect, but became apparent only when made visible at the margin of the bone by the process of modeling.

The "simple bone cyst" is a striking example of faulty enchondral bone formation (Fig. 10). This lesion exhibits no autonomous growth, and does not expand the bone. The width of a simple cyst is usually no greater than that of the metaphysis at the time it was formed. It is probable, however, that the submetaphyseal cyst is a considerably more complex lesion than a simple abnormality of conversion of cartilage into bone. If an attempt is made to cure a simple cyst by curettage and implantation of bone grafts when the nonosseous material still extends to the metaphysis, there may be resorption of the implanted chips and recurrence of the defect. Once the cyst moves toward the shaft by longitudinal bone growth and submetaphyseal bone appears normal, very simple surgical methods will effect a cure. This suggests that there is a mechanism for bone resorption that is active during the formation of the cyst at the metaphysis (Fig. 11, *A* and *B*).

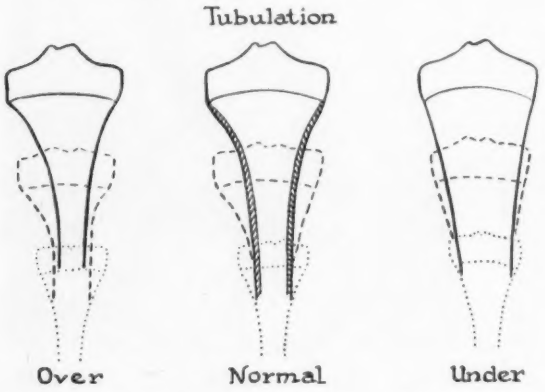


Fig. 13. Abnormal constriction or tubulation may be an important clue in roentgen diagnosis.

The residual of many simple conversion defects can be identified in the adult by the circumscribed deposit of calcium that occurs in later life.

To a large extent contour of a bone is dependent upon the stress applied to it. This phenomenon can be observed in fractures that have healed in faulty position,

or in epiphyseal separations with great displacement where a new shaft is formed from the massive subperiosteal hemorrhage with resorption of the unwanted portion of the original diaphysis. Our experience would suggest that normal stress applied to a malunited fracture will produce eventual restitution to the normal if a sufficient period of growth remains, and if the fracture occurs through a portion of the shaft where tubulation of the bone is being actively carried out (Fig. 12, *A* and *B*). However, if unusual or torsional stress is applied to the bone adequate straightening of the bone will not occur.

Abnormalities of the process of tubulation (Fig. 13) are a prominent feature of a number of diseases.[2] Of many of these conditions we have little knowledge, but only the ability to apply a name and such is Pyle's disease,[10] the first example of which was a single femur from an archaic Nubian graveyard.[13] Here is gross failure of tubulation without known etiology (Fig. 14). It may be associated with abnormalities of the skull and facial bones, very similar to those observed in polyostotic fibrous dysplasia (Fig. 15). When one examines the roentgen abnormalities that arise from aberrations of growth it soon becomes evident that identical patterns are produced by a variety of etiologies. The failure of tubulation of the bone associated with Gaucher's disease (Fig. 16) simulates closely the Erlenmeyer flask appearance of of Pyle's disease, and in many patients infiltration of the neck of the femur with Gaucher cells will produce diminution in blood supply to the femoral head, causing changes roentgenographically indistinguishable from Legg-Perthes' disease (Fig. 17). A patient immobilized in a frog-leg position for reduction of congenital dislocation of the hip may develop similar changes from the diminution of blood flow produced by torsion of the vascular retinaculum of Weitbrecht. Enchondral bone formation can probably be distorted by innumerable genetic or environmental factors of which we know nothing. We do

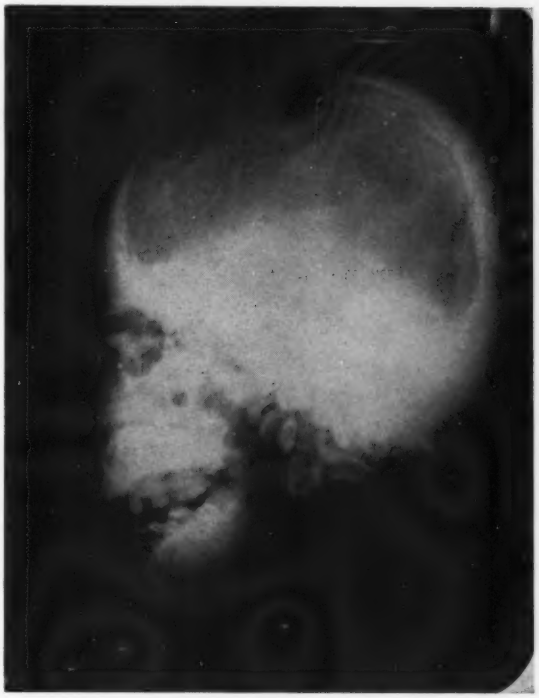


Fig. 15. Roentgenogram of the skull of the patient whose femora are shown in Figure 14. The appearance suggests a fibrous dysplasia.

Fig. 14. Striking failure of tubulation. "Pyle's disease?"

Fig. 16. Defective tubulation in a patient with Gaucher's disease. A similar appearance may be seen associated with chronic leukemia in childhood.

Fig. 17. Bilateral coxa plana evidently produced by diminution of blood supply from infiltration of Gaucher cells about the femoral neck and capsule.

Fig. 18. Abnormal development of vertebral bodies produced by irradiation by roentgen rays. The appearance is similar to that associated with the osteochondrodystrophies.

know that roentgen and clinical entities can be produced by clinically administered agents. Roentgen radiation if given in sufficient quantities to the developing spine of a young infant will produce localized abnormality of growth which will vary from

Fig. 19. An exostosis of the left ilium apparently produced by roentgen irradiation.

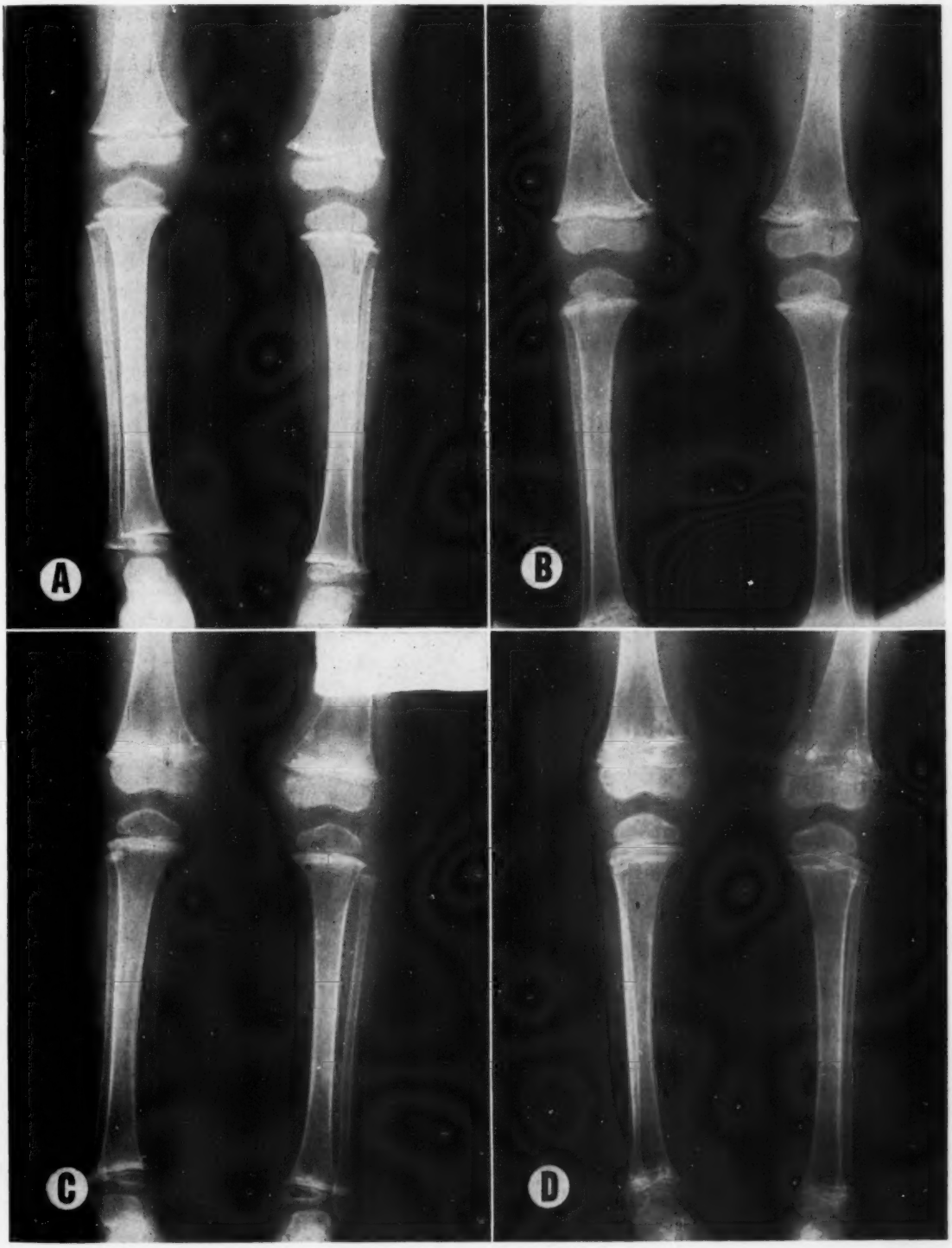


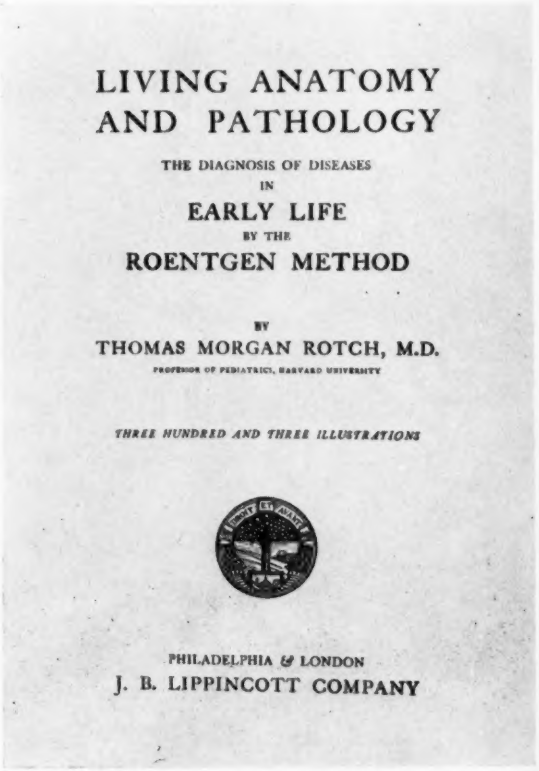
Fig. 20. (*A*) (*B*) and (*C*) Prolonged administration of "aminopterin" to this patient produced a remission of the leukemia. The progressive loss of density of the bone and alteration of metaphyseal architecture is evidently produced by the "antifolic acid" compound. Longitudinal growth appears to be progressing at a satisfactory rate.

FIG. 21. The narrow aganglionic segment of colon characteristic of Hirschsprung's disease may eventually disappear from the impact of fecal mass.

bands of increased density or slight irregularity of contour to changes that are quite indistinguishable from the characteristic changes of the osteochondrodystrophies (Fig. 18). Roentgen irradiation may produce non-resorption exostosis (Fig. 19). Chemical compounds administered in the treatment of disease may produce roentgen changes that will closely simulate other conditions. The group of drugs called antifolic acid antagonists, used in the treatment of leukemia, have been observed to produce progressive diminution in density of bone and metaphyseal and submetaphyseal fractures that will cause symptoms suggesting recurrence of the bone pain of leukemic infiltration (Fig. 20, *A*, *B*, *C* and *D*). The lesions produced by long continued administration of aminopterin may closely resemble scurvy.

Even in this brief examination it should be clear that the impacts of growth on disease may produce changes in the pattern of disease. In these changes one can recognize the mechanism of the production of many abnormalities which in the adult are observed only in the end stage, often partially obscured by degenerative processes. For example, in Hirschsprung's disease in the infant or young child the narrowed aganglionic segment of bowel with the proximal hypertrophy can be identified (Fig. 21), but with the constant stress and impact of fecal masses upon the aganglionic segment eventual dilatation of this segment probably occurs so that one has, as an end result, a total megacolon.

In 1910 the first textbook of Pediatric Radiology, based upon an experience of over twenty-three hundred patients, was written by Thomas Morgan Rotch[12] (Fig. 22). Then for thirty-five years there ensued what Doctor Caffey has called "the great pediatric literary hypoplasia," which his text has done much to rectify. This field


LIVING ANATOMY
AND PATHOLOGY

THE DIAGNOSIS OF DISEASES
IN
EARLY LIFE
BY THE
ROENTGEN METHOD

BY
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PROFESSOR OF PEDIATRICS, HARVARD UNIVERSITY

THREE HUNDRED AND THREE ILLUSTRATIONS

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FIG. 22. The first textbook of Pediatric Radiology in English was published in 1910.

is still relatively unexplored. There is lack of appreciation of its significance by the majority of physicians. Many are prone to react as did Dr. Soma Weiss, Professor of Medicine at Harvard, when called in consultation to examine an infant patient, his only remark was, "Yes, we see that condition in humans too." We trust that this is now an attitude of the past. To a great extent the pathogenesis of disease can be elucidated only by a study of the conceptus and the genetic background, and only by a thorough examination of the developing child in relation to his inheritance and to his environment. This is not work completed; it is the challenge of Pediatric Radiology for the future.

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AN UNUSUAL CASE OF INTRATHORACIC FIBROMA ASSOCIATED WITH PULMONARY HYPERTROPHIC OSTEOARTHROPATHY

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INTRATHORACIC fibroma is an extremely rare tumor. Blades[3] in 1941 surveyed the literature extensively and found only 32 cases reported. In 1940, Susman[22] described a case of a huge intrathoracic fibroma in which no definite point of origin could be found. Clagett and Hausmann[5] reported a similar case in 1944.

The case being published here is unusual in two respects: First, its presence dates back at least twenty-two years, as proved by a chest roentgenogram taken in 1929. Second, marked hypertrophic pulmonary osteoarthropathy was present at the time of admission. Although hypertrophic osteoarthropathy is occasionally associated with pulmonary neoplasms, we were unable to find any mention of its presence in the previously reported cases of intrathoracic fibromas.

Intrathoracic fibromas possess the features of all benign tumors, being usually encapsulated and lacking the invasive tendencies of malignant tumors. They may originate from the structures of the mediastinum, the lungs, the visceral pleura, the parietal pleura or from any tissues of the thoracic wall or vertebrae. It may often be difficult to find the point of origin, especially when the tumor is large and adherent to several structures. Heuer and Andrus[16] state that fibromas and neurofibromas are the most silent tumors of the thorax. Only when the tumor has reached considerable proportions are symptoms produced. Therefore, small tumors of this kind are usually detected in routine roentgen examination of the chest. When symptoms do occur, they are the result of pressure, such as productive or nonproductive cough, dyspnea and thoracic pain. In addition, engorgement of the veins of the upper extremity and neck may be noticed.

As mentioned above, hypertrophic osteoarthropathy is not a rare accompaniment of pulmonary neoplasms. The most commonly associated condition is a bronchogenic carcinoma, and in many of these cases the symptoms of hypertrophic osteoarthropathy were present months or years before the symptoms of pulmonary disease (Craig,[6] Pattison and co-workers[21]). Besides being associated with chronic pulmonary conditions, hypertrophic osteoarthropathy has been reported in diseases of the heart, liver, blood, thymus, gastrointestinal tract and nasopharynx.

There are many theories as to the etiology of hypertrophic osteoarthropathy and numerous papers have been written on these theories. They may be summarized briefly as follows:

1. Chronic increased blood flow with increased periosteal nutrition.
2. Dysfunction of the pituitary gland.
3. Decrease in oxygen tension of the blood with poor oxygenation.
4. Reduced surface area of the erythrocytes with impaired oxygen release to the tissues (Mauer's theory).
5. Toxic absorption of the infection from widened and infected bronchi with subsequent subperiosteal irritation.

The bone changes observed in hypertrophic osteoarthropathy are those of chronic proliferative subperiosteal osteitis surrounding the shafts of the involved bones. The new bone formation varies in thickness from 1 to several millimeters and consists of cancellous tissue covered by a thin cortex. This new bone is extremely vascular, soft and pliable, and easily cut or torn away from the old cortex.

The most commonly involved bones are the distal portions of radiuses, ulnas, tibias and fibulas. In addition, the metacarpal and metatarsal bones are frequently affected. In advanced cases, the spines of the scapula and the vertebrae may also be involved. A characteristic sign which can be clinically observed is the clubbing of fingers which is probably due to thickening of the connective tissues; however, the terminal phalanges may also show some absorption. The synovial membranes of the joints may often reveal lymphocytic infiltration.

The symptoms of this condition usually simulate those of arthritis. Aching pains, tenderness of bones and joints, muscular weakness, burning sensations are the most frequent complaints of the patients. Clinical signs of noninflammatory swelling of the joints are commonly observed. This is often associated with edema and hypertrophy of the subcutaneous tissues. As previously mentioned, clubbing of fingers and toes is one of the outstanding clinical signs. Occasionally, increased sweating of the hands and feet and gynecomastica may develop.

Roentgenologic examination in hypertrophic osteoarthropathy reveals irregular periosteal accretions of new bone along the shafts of the long bones and along the periphery of the larger bones of the pelvis and shoulder girdle. The periosteal "involucrum" appears to develop in thickness with the size of the bones, being thickest in the femur and narrowest in the middle phalanges.

The condition tends to develop first in the distal portions of the long bones and later in a proximal direction toward the mid-shaft. The periosteal response is usually much less dense than the cortex, and its surface, as a rule, is irregular and sometimes woolly in appearance. The terminal phalanges do not show any hypertrophic reaction, although in some cases irregularity of the terminal cancellous tuft is seen. No irregularity of the articular surfaces or of the periphery of the carpal and tarsal bones is noted. Osteoarthropathy is usually associated with some degree of osteoporosis of all bones.

REPORT OF A CASE

F. B., male, aged sixty, iceman, was admitted to the Flower and Fifth Avenue Hospital on May 12, 1951, giving the following history: In 1929, he was seen by a physician because of a nonproductive cough. A roentgenogram of the chest revealed a tumor mass about 5 by 10 cm. in size located in the left hemithorax

Fig. 1. Roentgenogram of chest (taken in 1929) reveals a large soft tissue mass in the left mid-lung field. (A lateral view was not available.)

(Fig. 1). His cough, however, disappeared, and he sought no further treatment. During the next several years, the cough returned intermittently, but never became very severe.

During one of his episodes of a nonproductive cough in 1945, a second chest roentgenogram was taken, and the tumor was found to have grown considerably (Fig. 2). According to the patient, surgery was never recommended by any of the many physicians he had consulted. About one year later, the patient noticed painful swelling of his ankles and wrists with broadening of the finger nails. All these changes became so pronounced during the last two years

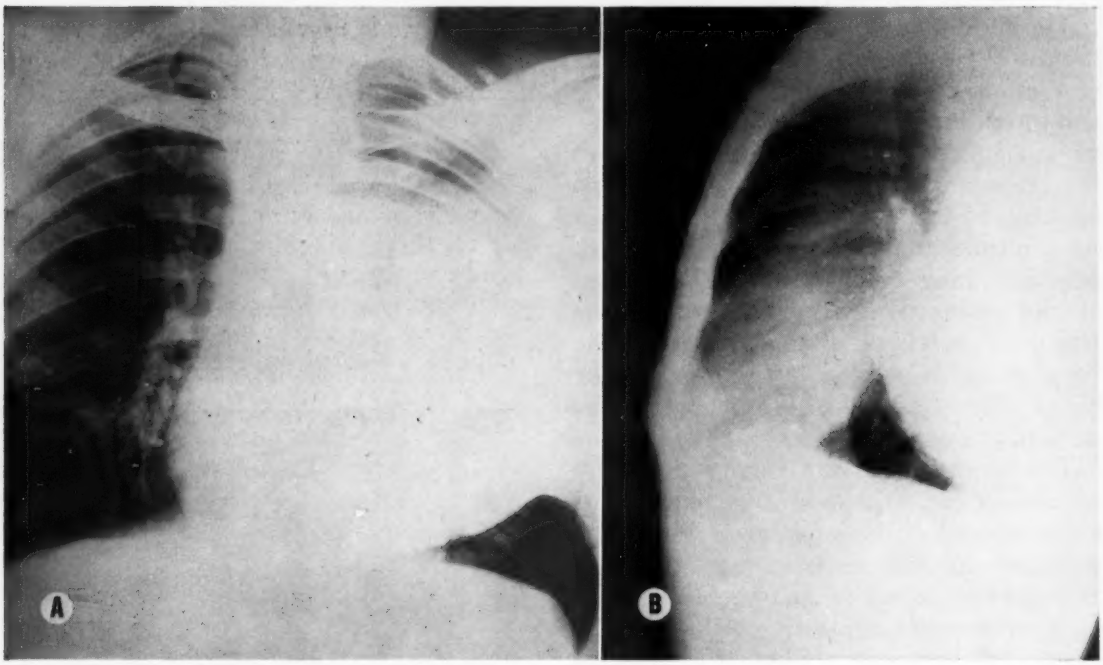

FIG. 2. (*A*) Roentgenogram of chest (taken in 1945) reveals a marked increase in size of the tumor located in the left hemithorax. Note sharp contours and partial atelectasis of left upper lung field. (*B*) Left lateral view reveals the tumor mass to be located in the lower posterior portion of the left thorax.

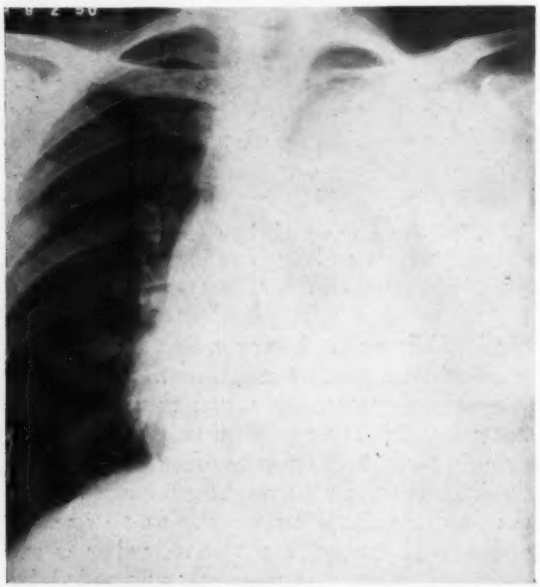

FIG. 3. Roentgenogram of chest (taken in August, 1950) reveals a further increase in the size of the tumor which occupies almost the entire left hemithorax. Note displacement of the heart and trachea toward the right.

that the patient was forced to give up his work.

In August, 1950, another roentgenogram of the chest was taken and showed a further increase in the size of the tumor (Fig. 3). At that time, the patient was moderately dyspneic but complained mainly of the pains in his legs and arms. Surgery was recommended but rejected by the patient at this time; however, nine months later, all symptoms and signs increased in severity and the patient finally submitted to surgical intervention.

At the time of admission, the patient complained of severe pains in his knees, ankles and wrists, dyspnea and exertion, hoarseness and a slight cough productive of whitish sputum.

Physical Examination. This examination revealed a well nourished white male with no cyanosis. The positive physical findings were a dilated left pupil, deviation of the trachea to the right, dullness and absence of breadth sounds over the entire left lung field, shifting of the heart to the right and marked clubbing of fingers and toes (Fig. 4). Blood pressure readings were as follows: right arm 136/66, left arm 128/58, right leg 166/68, left leg 178/80.

Laboratory Findings. Electrocardiogram, no abnormal features. Blood count: Hemoglobin 88 per

cent; red blood cell count, 4,470,000; white blood cell count, 9,600, with 70 per cent neutrophils (mature), 1 per cent eosinophils, 26 per cent lymphocytes and 3 per cent monocytes.

Urine, negative (5/14/51).

Alkaline phosphatase 8.5 King-Armstrong units (normal) (5/14/51).

Acid phosphatase 3.6 K.A. units (normal) (5/14/51); 7.8 K.A. units (high) (5/28/51); 12.6 K.A. units (high) (9/4/51).

Cephalin flocculation, negative.

Thymol turbidity, 2 units.

Eagle Wassermann, positive; flocculation test, negative; interpretation, doubtful.

CO_2 combining power, 56 vol. per cent; cholesterol, 180.4 mg.; icterus index, 5; bilirubin, 0.3; serum proteins, 6.52 (albumin, 3.94; globulin, 2.58); urea, 13.1; nonprotein nitrogen, 28.7; sugar, 74.9; creatinine, 1.31; sodium, 293.25; potassium, 15.4; calcium, 10.7; phosphorus, 3.08 mg.

Fig. 4. Photograph of patient's hands at admission (May, 1951) shows marked swelling of soft tissues and clubbing of fingers.

Roentgenographic Examination. Chest: Large tumor mass occupying almost the entire left hemithorax with displacement of the heart and mediastinum toward the right. Slight aeration of the left lung present only in the apex and anterior aspect of the upper portion. Right lung clear (Fig. 5, *A* and *B*). Laminagrams of the chest revealed, in addition to the large tumor mass, slight erosion of the lateral aspect of the bodies of the upper thoracic vertebrae on the left side. There was marked displacement of the trachea toward the right. Bronchography: No lipiodol entered the left bronchial tree. Right bronchial tree appeared normal. Extremities: Extensive irregular periosteal thickening of femurs, tibias, fibulas, humeruses, radiuses, ulnas and metacarpal and metatarsal bones (Fig. 6, *A* and *B*).

Operative Findings. May 29, 1951. Left thoracotomy, removal of tumor, left pneumonectomy under pentothal anesthesia. A few

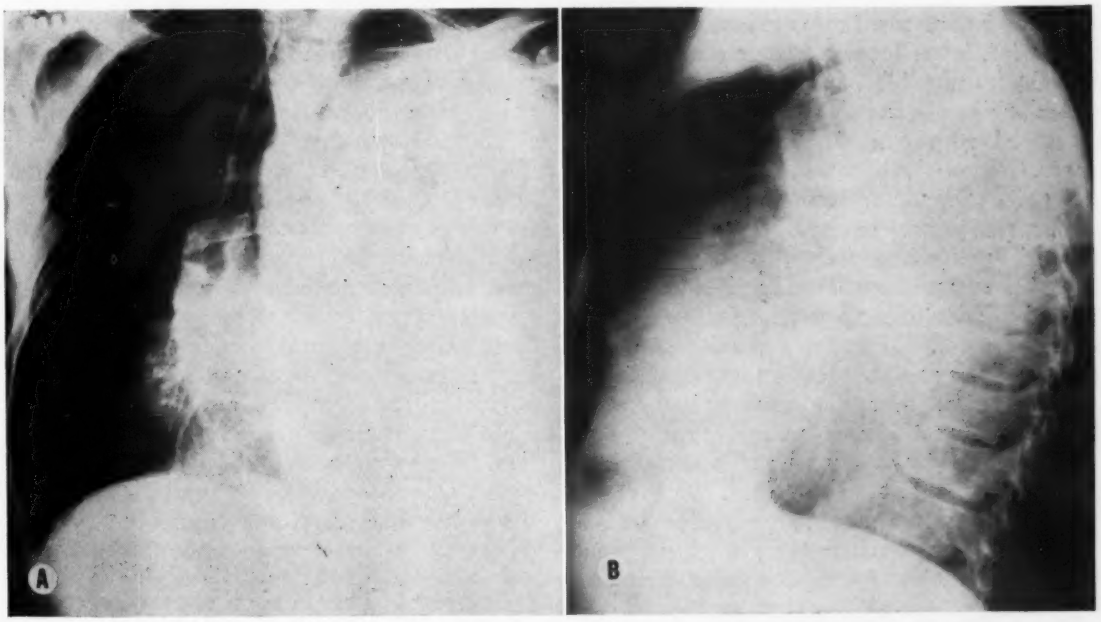

Fig. 5. (*A*) Roentgenogram of chest (taken in May, 1951) shows a further increase in size of the tumor indicated by a marked displacement of the trachea toward the right. Only a small area of the left apex is aerated. (*B*) Left lateral view reveals the tumor occupying the posterior three-quarters of the left thorax.

FIG. 6. (*A*) Roentgenogram of forearms (taken in May, 1951). The periosteum of the lower humerus, radius and ulna is markedly thickened and ossified with irregular and wavy outlines. (*B*) Roentgenogram of hands (taken in May, 1951). Similar changes are noted in the periosteum of the metacarpal bones and the phalanges. In addition, there is expansion of the soft tissues surrounding the terminal phalanges and hypertrophic changes of the tufts.

pleural adhesions were released by blunt dissection. A tumor mass approximately 14 inches in length and 8 inches in width was found to be present. It was markedly adherent to the left lower lobe and somewhat adherent to the left upper lobe. It was adherent by small adhesions to the cupola and seemed to derive its blood supply from the posterior pleural space. Otherwise, the mass did not seem to have a definite pedicle and seemed to be completely within the pleural cavity. The mass was well defined, well encapsulated, appeared benign, and was removed by sharp and blunt dissection. A portion of the lower lobe was definitely atelectatic and did not re-expand well on inflation. A left pneumonectomy was done.

Gross and Microscopic Pathological Report. Large, completely encapsulated tumor mass measuring 23 by 20 by 14 cm. and weighing 3.100 grams (Fig. 7, *A* and *B*). The capsule is intact and shows a small vascular pedicle measuring 3 cm. in diameter. On section, various sized nodules of compact tissue separated by bands of soft adenomatous connective tissue were seen. The nodules ranged from 1 to 8 cm. in diameter and some of the larger nodules showed extensive central necrosis with pseudocystic changes. Most of the nodules consisted of firm, white, striated tissue while the smaller nodules toward the periphery had a myxoid appearance. Microscopic diagnosis: Fibroma (Fig. 7*C*). Left lung: Focal compression atelectasis with marked fibrosis and recent hemorrhage. Hilar nodes: Anthracosis and fibrosis.

The postoperative course was uneventful. The patient developed a hydropneumothorax on the left side. Roentgen examination of chest (ten days after operation) showed a horizontal fluid level in the upper two-thirds of the left thorax. The left apex and infraclavicular region revealed a structureless area of illumination (air). The heart and mediastinum were in normal position. The patient was discharged on June 16, 1951, in good condition.

He was last seen four months after the operation. The swelling of the legs had diminished with a gain in weight of 6 pounds. The pain in the wrists, knees and ankles and the dyspnea on exertion were no longer present.

Comment. The benign character of the tumor in this case was evidenced by a slowly expanding growth over a period of more than twenty years and by the roent-

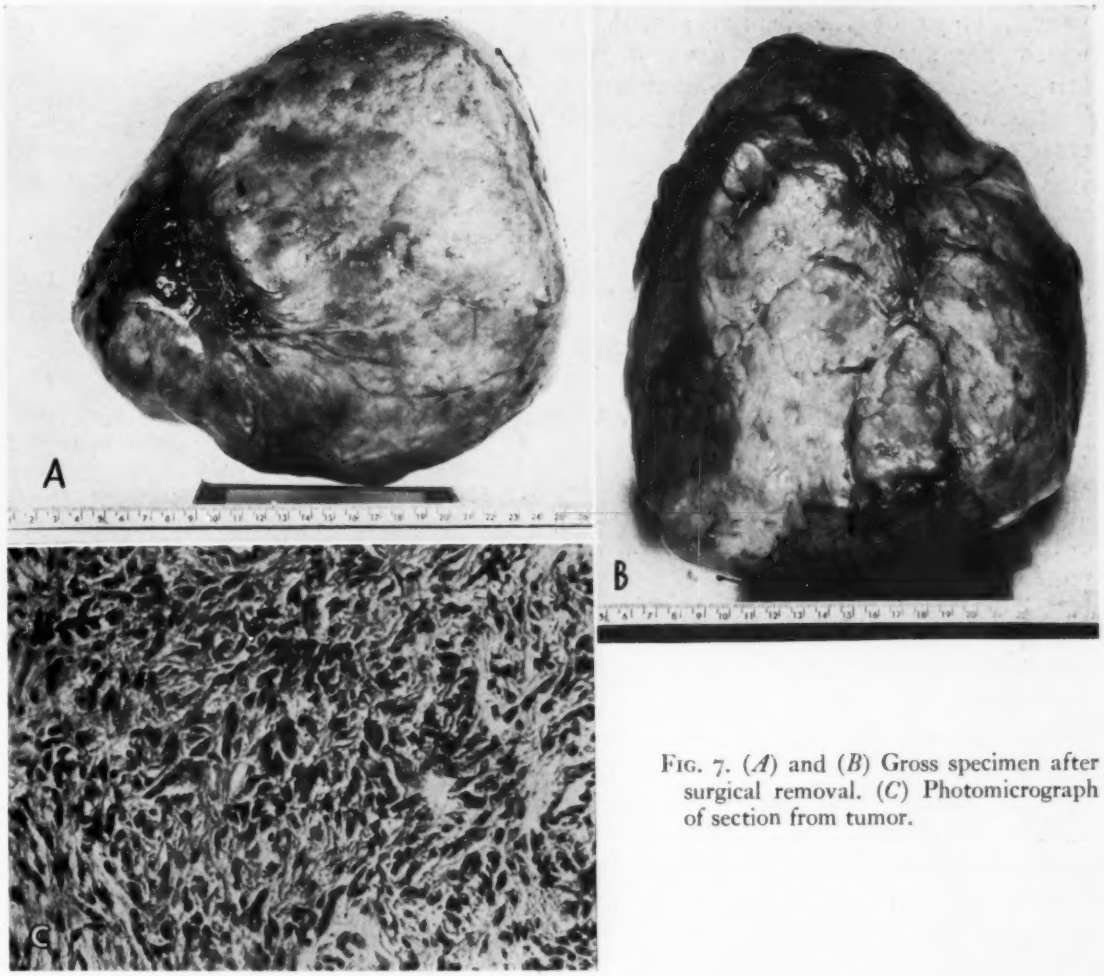

Fig. 7. (*A*) and (*B*) Gross specimen after surgical removal. (*C*) Photomicrograph of section from tumor.

genological appearance of the mass which revealed sharply defined, smooth outlines, a homogeneous structure and a lack of infiltration or invasion into the surrounding tissues. Although a roentgenologic diagnosis of a fibroma could not be made, since the tumor was located in the posterior portion of the left thorax, a preoperative diagnosis of a neurofibroma was ventured. Nevertheless, histopathologically no neurogenic elements could be found in any of the sections.

Another point of interest is the pathogenesis of the associated hypertrophic osteoarthropathy in the case reported here. Craig[6] has stated that the occurrence of symptoms of hypertrophic osteoarthropathy often precedes the detection of a pulmonary neoplasm. This may apply only to cases of malignant neoplasms. In the case described here, the tumor was first discovered twenty-two years before the operation, whereas the swelling of the extremities and the pains in the knees, ankles and wrists developed only within the last four years at which time the intrathoracic tumor had reached considerable size. Therefore, with the presence of a benign intrathoracic tumor, the pathogenesis of hypertrophic osteoarthropathy may best be explained by an impairment of the pulmonary vessels due to mechanical pressure of the tumor which leads to a decrease in oxygen tension and consequent poor oxygenation of the blood. These changes, however, take place in an ad-

vanced stage of the benign growth in which the symptoms and signs of the intrathoracic tumor have become apparent long before the development of the bone changes.

SUMMARY

A case of an intrathoracic fibroma, originating from the posterior pleura, with several unusual features is presented.

1. Evidence of its existence for more than twenty-two years.

2. The tumor was unusually large, occupying almost the entire left hemithorax and exerting marked pressure upon the heart and mediastinal structures. In spite of its size a successful surgical removal was possible.

3. The tumor was associated with pulmonary hypertrophic osteoarthropathy. This is, to our knowledge, the only case in the literature in which an intrathoracic fibroma produced changes of hypertrophic osteoarthropathy.

4. An attempt has been made by the authors to explain the pathogenesis of osteoarthropathy in cases of benign intrathoracic tumors.

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We wish to extend our thanks to Dr. F. J. Borrelli in particular and to Dr. S. Thompson, Dr. F. Speer, Dr. M. Silverstein and Dr. H. Parnas for their cooperation.

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Vol. 69, No. 5

VISUALIZATION OF THE COMMON DUCT DURING CHOLECYSTOGRAPHY

ITS SIGNIFICANCE*†

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CLEVELAND, OHIO

WITH the introduction of cholecystography by Graham and Cole in 1924, another door was opened in the physician's diagnostic armamentarium. Several excellent reports appeared soon thereafter in the literature concerning the physiological aspects of cholecystography. However, these were lost among the many descriptions of positive findings such as opaque and nonopaque calculi, tumors and so-called "nonfunctioning gallbladders." In this type of examination, even disregarding the gallbladder physiology, it is generally conceded that the accuracy of cholecystography is approximately 94–97 per cent.

There is a significant number of gallbladder examinations reported as "normal functioning gallbladder", despite the symptomatology referable to the biliary system. Many patients with such reports are eventually subjected to a cholecystectomy, with the removal of a normal gallbladder, and no permanent relief of symptoms. It is in regard to this important group of patients that the present study has been made. Undoubtedly, the 20–25 per cent poor results following surgery on these patients contribute to many of the failures of gallbladder surgery. Rightfully, such instances should not be classified as postcholecystectomy complications or syndromes, for they had existed prior to surgery.

Only as we follow and understand the precepts of our former teachers, through the application of a thorough knowledge of roentgen anatomy and roentgen physiology, may we hope to be able to recognize the pathological changes of the biliary tract.

ANATOMY

That anatomy which concerns the physiological aspects of the biliary tract is briefly reviewed (Fig. 1). The gallbladder

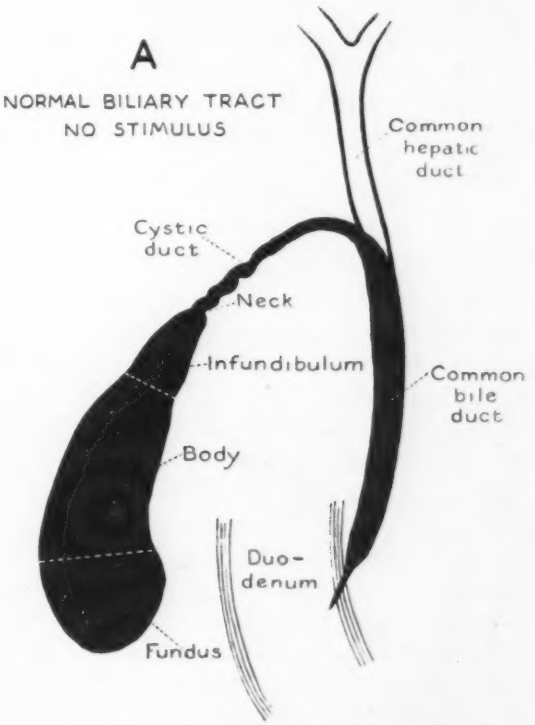

FIG. 1. Normal anatomy of the extrahepatic biliary tract.

* From the Radiological Service, Veterans Administration Hospital and Western Reserve University School of Medicine, Cleveland, Ohio. Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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is made up of a fundus comprising the distal third, the corpus the middle third and the infundibulum (Hartmann's pouch) the remainder. The gallbladder serves as a reservoir; and, during contraction, expels the bile into the cystic and common duct. The wall of the fundus and infundibulum is made up of a fibromuscular layer, whereas the wall of the body is rich in elastic fibers. There is a sphincter, or sphincter-like, mechanism involving the junction between the infundibulum and cystic duct known as Lütken's sphincter.

For practical purposes, there are no muscle fibers in the cystic, hepatic and common ducts; and no peristalsis has ever been demonstrated. The cystic duct is comprised of a valvular portion, Heister's valves, and a smooth portion called the pars glabra. It forms a gradual curve as it extends up from the neck of the gallbladder and joins with the common hepatic duct to form the common duct.

The common duct extends in a gentle curve, with its convexity to the left, sometimes overlying the spine, and inserts into the medial posterior aspect of the descending duodenum. The common duct may be divided into three parts: supraduodenal, pancreatic and transduodenal (sphincter of Oddi, or that which Ivy and others refer to as the choledochoduodenal) junction. The choledochoduodenal junction, according to Ivy, consists of four intrinsic muscles (Fig. 2): (1) two longitudinal oblique bundles which tend to shorten the duct and erect the papilla; (2) an annular sheath (sphincter choledochus) which surrounds the common duct where it enters the duodenum to where it joins the pancreatic duct; (3) an annular sheath which surrounds the pancreatic duct before it joins the common duct (a pancreatic sphincter is present in one-third of individuals), and (4) an annular sheath which surrounds the ampulla corresponding to the papillary sphincter described by Westphal.

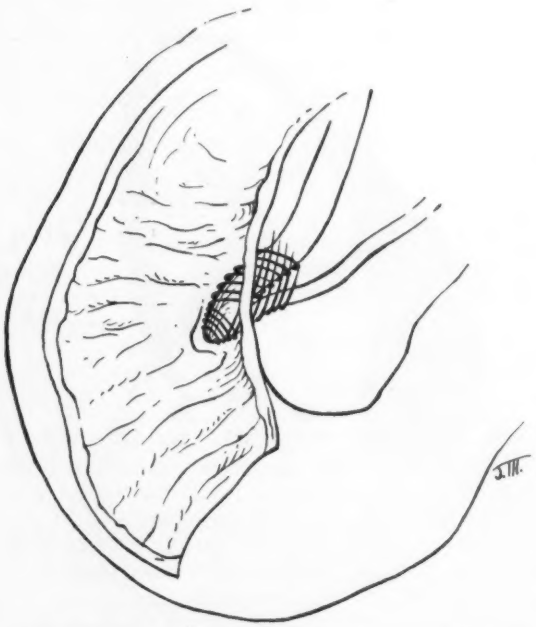


FIG. 2. Anatomy of the choledochoduodenal junction showing: two longitudinal bundles; annular sheath (sphincter choledochus) encircling the common duct; annular sheath (sphincter pancreaticus) surrounding the pancreatic duct, and annular sheath surrounding the papilla.

PHYSIOLOGY

The average secretory pressures of the liver and pancreas are about the same—between 30 and 35 cm. of water. The intraluminal pressure of the common duct is between 8 and 12 cm. of water and is dependent on the tone of the sphincter of Oddi. The intraluminal pressure of the gallbladder in a resting stage is 10 cm. of water and during contraction is 25 cm.

Under normal conditions, the bile produced in the liver is transported by the biliary ducts at a pressure of approximately 8 to 12 cm. of water. The bile is stored in the gallbladder at a pressure slightly below the common duct pressure. Fats, acids, or partially digested proteins in the duodenum, stimulate the mucosa to produce a hormone which Ivy calls cholecystokinin. This substance causes the gallbladder to contract, raising its pressure to as high as 20 to 25 cm. of water forcing the bile to flow into the duodenum. In addition, a reciprocal relationship exists between the gallbladder contractions and the opening of the sphincter of Oddi. The sphincter, or

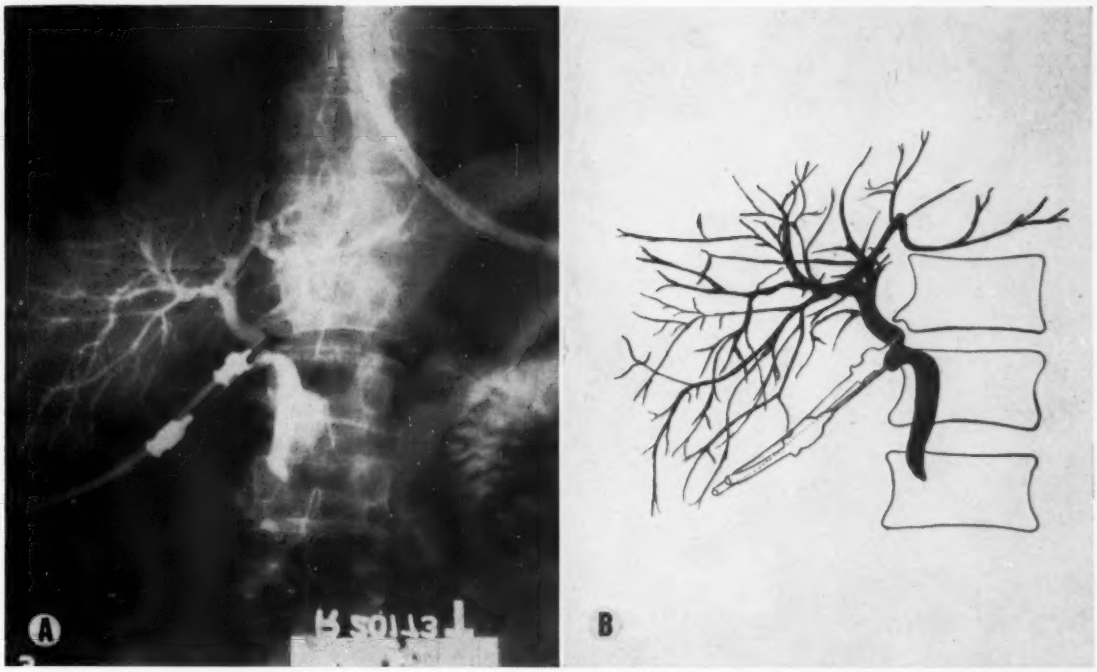


Fig. 3. Spasm of the sphincter of Oddi. B. H., operative cholangiogram after the slow injection of 15 cc. of an aqueous contrast medium showing complete obstruction of the transduodenal segment of the common duct with minimal proximal dilatation. The fine intrahepatic radicles are filled with contrast medium. Common duct pressure at this stage was 60 cm. of water. (From Cholangiography, Surgical Monograph, 75–149, 1951. Courtesy of Thomas Nelson & Sons, New York.)

sphincter-like mechanism of Lütken may also play a part in the reciprocal action. Under normal conditions, the contracting gallbladder does not produce a reflux into the common hepatic duct.

According to Ivy, all animals with a gallbladder possess a sphincteric mechanism at the choledochoduodenal junction which is coordinated with duodenal tone and motility but may act independently. Resistance of the sphincter of Oddi to the flow of fluid into the duodenum may reach as high as 75 cm. of water. If this resistance causes a rise in intraductal pressure much above 20 cm. of water, pain may ensue. This has been observed during operative cholangiography under spinal anesthesia. If the resistance is prolonged with marked narrowing of the transduodenal segment of the common duct, proximal dilatation of the common duct as well as the intrahepatic radicles occurs (Fig. 3).

Westphal described a series of experiments in which the vagus was stimulated with three different strengths of faradic current (Fig. 4): weak, moderate and marked. With a weak current, there was contraction of the gallbladder, peristalsis of the antrum, and relaxation of the papilla of Vater. With a moderate current, the gallbladder contractions became somewhat vigorous and ampullary tone increased so that the gallbladder emptied more rapidly. With a marked vagal stimulation, the gallbladder contractions became marked and the sphincter of Oddi was thrown into spasm. The latter situation has been called hyperkinetic dyskinesia, while the second type has been referred to as hypertonic dyskinesia. Hill is of the opinion that, in addition to the hyperkinetic and hypertonic dyskinesia, there may also be an atonic dyskinesia. He believes that hyperkinetic dyskinesia due to strong vagal stimulation is associated with rapid gallbladder contractions, spasm of the

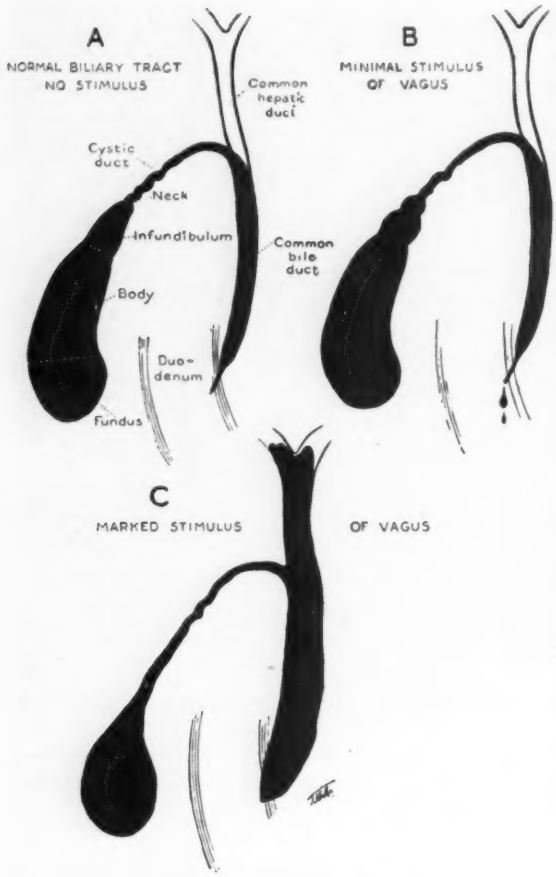


FIG. 4. Effects of vagal stimulation on the biliary tract. (*A*) Normal gallbladder and ducts prior to vagal stimulation. (*B*) As the gallbladder contracts there is peristalsis of the antrum and simultaneous relaxation of the papilla of Vater. (*C*) Marked gallbladder contractions with spasm of sphincter of Oddi resulting in dilatation of the common, hepatic and bile ducts.

sphincter of Oddi, distention of the common duct with subsequent pain, whereas, in atonic dyskinesia due to overstimulation of the sympathetic nerves, there is an atonic gallbladder, spasm of the papilla of Vater with a heavy aching sensation in the epigastrium. The two conditions could be differentiated by a careful history in correlation with cholecystography and duodenal intubation.

MECHANISM OF GALLBLADDER EMPTYING

It is difficult to evaluate evacuation time of the gallbladder as an indicator of motor function of the biliary tract. There is a wide range of variability in the time and extent of contractions following a fat meal. Although determination of the time interval in evacuation is significant, it is not as important as is the mechanism of emptying.

Two types of contraction have been described in the gallbladder. There are rhythmic contractions involving one to several segments or the entire gallbladder at a rate of two to six per minute. There are also tonic contractions which cuase a rise in pressure lasting five, thirty and sometimes forty-five minutes.

Boyden described emptying of the gallbladder in the cat as taking place in three phases during one hour and forty minutes. The first phase was one of slow emptying. This was followed by a period of rest and then of refilling in the third phase. Higgins and Mann stated that within fifteen to twenty minutes following the ingestion of food, several areas of contraction of the gallbladder could be seen. There were localized contractile areas which appeared at first independent of each other but which gradually merged to effect a reduction of the gallbladder of approximately 50 per cent, within a period of one and one-half hours. They also noted small knob-like diverticula produced by the contractions. Sussman stated that from three to six hours were required for the gallbladder to empty.

Evacuation of the gallbladder may be summarized as occurring in three or more phases. In the first and most important phase, the gallbladder contractions may be fairly vigorous, rhythmic contractions lasting as long as forty-five minutes. During this period, the gallbladder decreases 25 to 50 per cent in size. Following this initial contraction phase, there is a resting phase of one to one and one-half hours. The third phase of refilling of the gallbladder is immediately followed by a second contraction period. As the process repeats itself, each time the gallbladder contractions and evacuation become less; and

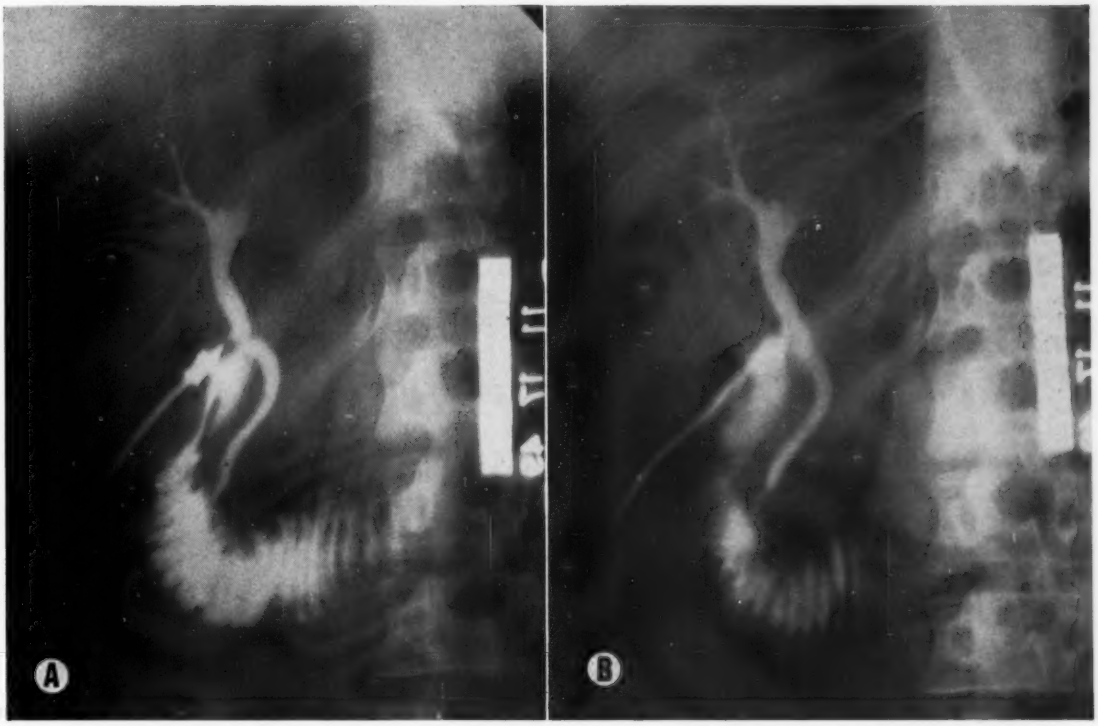


FIG. 5. Effect of morphine on the sphincter of Oddi. S. H., a twenty-nine year old white male, with a history of recurrent sharp epigastric and periumbilical pain associated with nausea and vomiting. Cholecystectomy for acute cholecystitis sixteen months previously. There was considerable emotional disturbance. Morphine reproduced a typical attack of pain. Laparotomy disclosed the absence of the gallbladder and a normal common duct. (*A*) An operative cholangiogram shows a normal common duct. (*B*) An operative cholangiogram fifteen minutes after the intravenous administration of morphine shows spasm of the transduodenal segment of the common duct. (From Cholangiography, Surgical Monograph, 75–149, 1951. Courtesy of Thomas Nelson & Sons, New York.)

in approximately three, and in some instances, six hours, the gallbladder is about one-sixth its original size.

ROENTGEN EXAMINATION OF THE GALLBLADDER

The roentgen examination of the gallbladder has not changed since it was first described by Graham and Cole in 1924. The standard procedure has been the ingestion of an oral halogenated preparation, in most instances priodax, twelve hours prior to the examination. During this period, the patient abstains from any fatty foods. If the twelve hour film reveals a satisfactory gallbladder shadow, a fatty meal is given and a second film taken within one to two hours.

Although there have been many roentgenological innovations regarding the identification of calculi, the time sequence has never changed. This, despite the fact that earlier investigators were able to demonstrate conclusively that for a proper understanding of the mechanism of evacuation as well as for an adequate roentgenographic demonstration of the extrahepatic tract, the roentgen exposures would have to be made within the first contraction phase of thirty to forty-five minutes.

Sussman visualized the extrahepatic ducts in 75 per cent of the patients by taking films at ten, twenty and thirty minutes following a fat meal of three egg yolks in a small amount of milk. Bronner was also successful in demonstrating the biliary ducts by taking films at fifteen minute intervals following a fat meal.

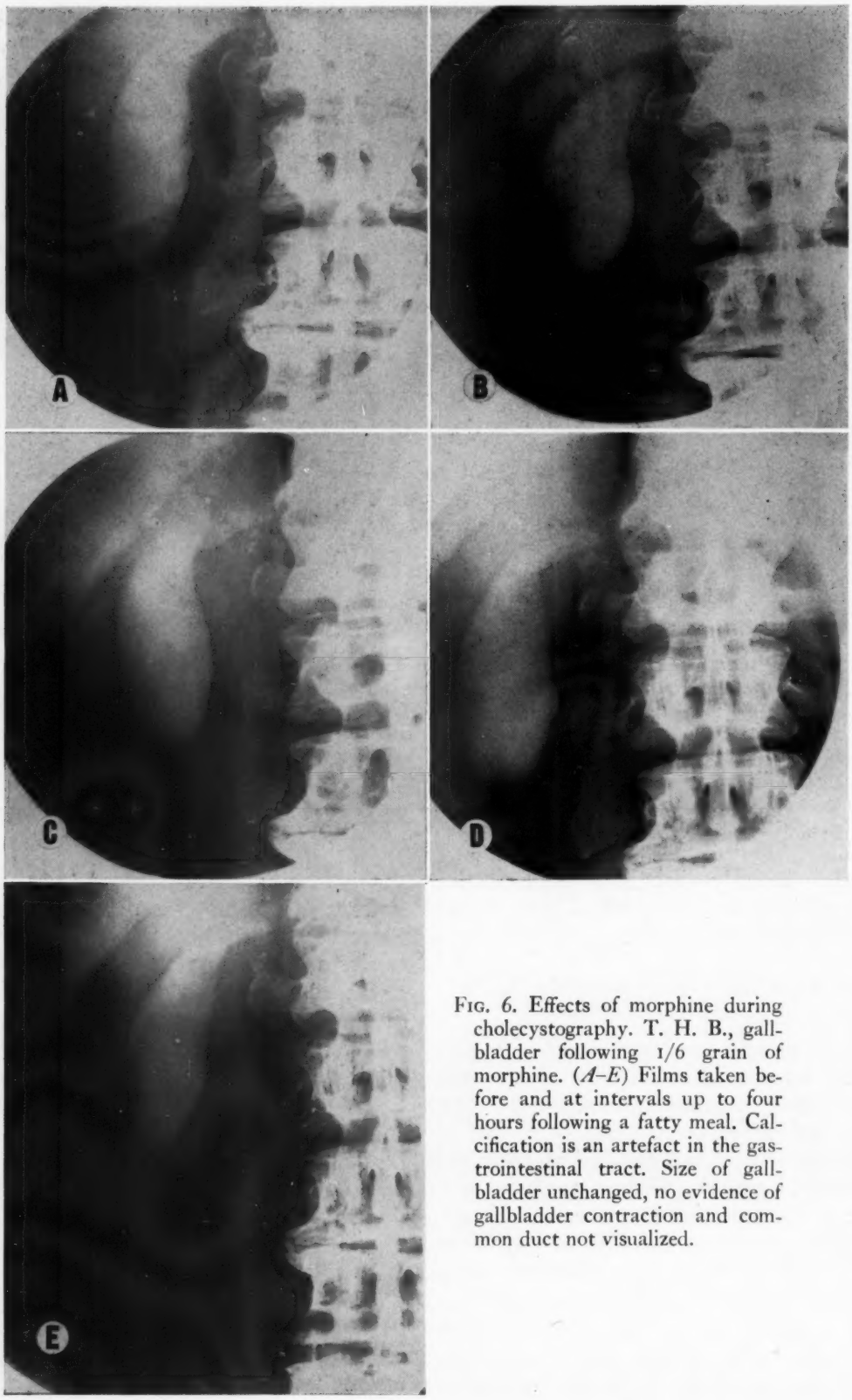


Fig. 6. Effects of morphine during cholecystography. T. H. B., gallbladder following 1/6 grain of morphine. (*A–E*) Films taken before and at intervals up to four hours following a fatty meal. Calcification is an artefact in the gastrointestinal tract. Size of gallbladder unchanged, no evidence of gallbladder contraction and common duct not visualized.

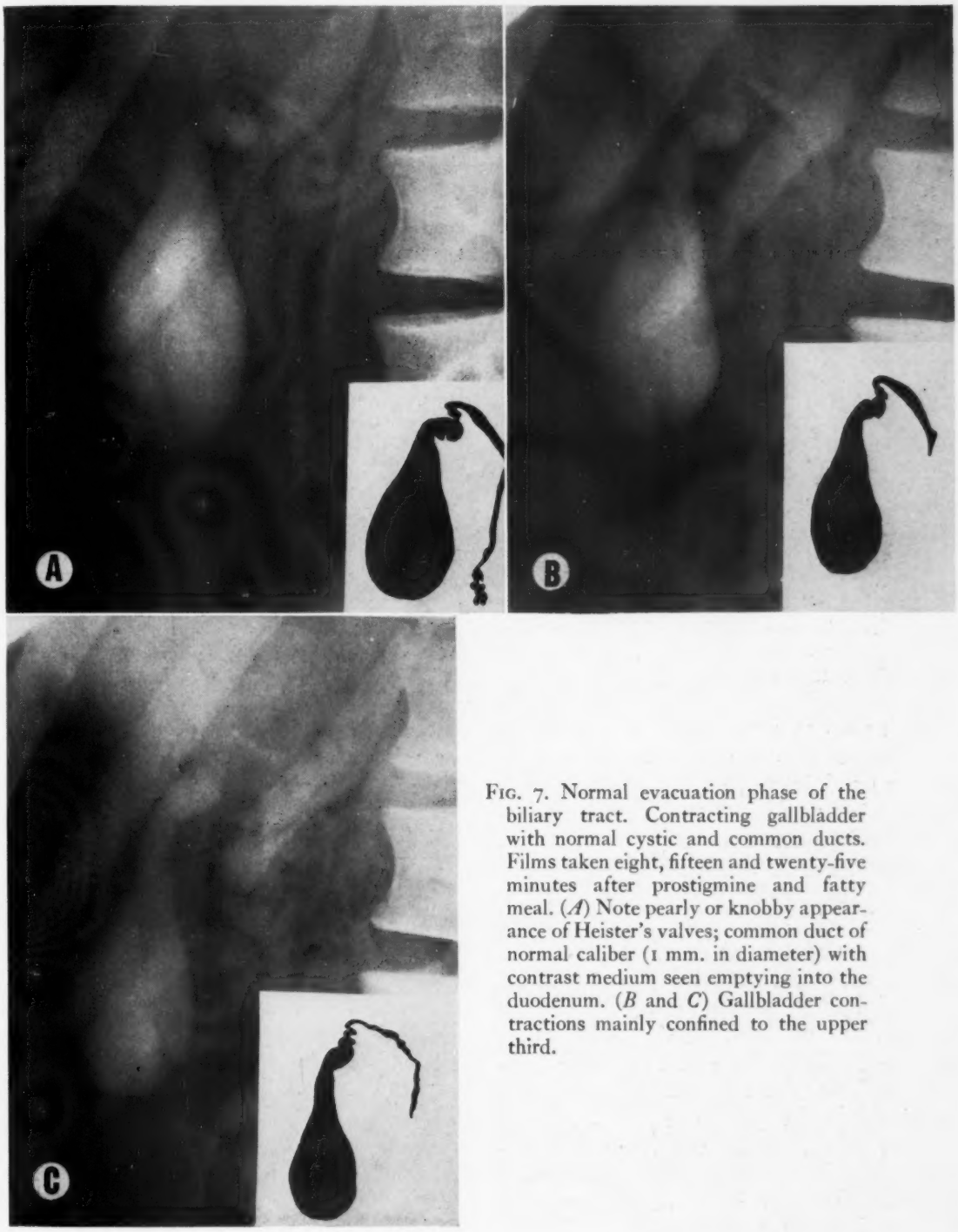


Fig. 7. Normal evacuation phase of the biliary tract. Contracting gallbladder with normal cystic and common ducts. Films taken eight, fifteen and twenty-five minutes after prostigmine and fatty meal. (*A*) Note pearly or knobby appearance of Heister's valves; common duct of normal caliber (1 mm. in diameter) with contrast medium seen emptying into the duodenum. (*B* and *C*) Gallbladder contractions mainly confined to the upper third.

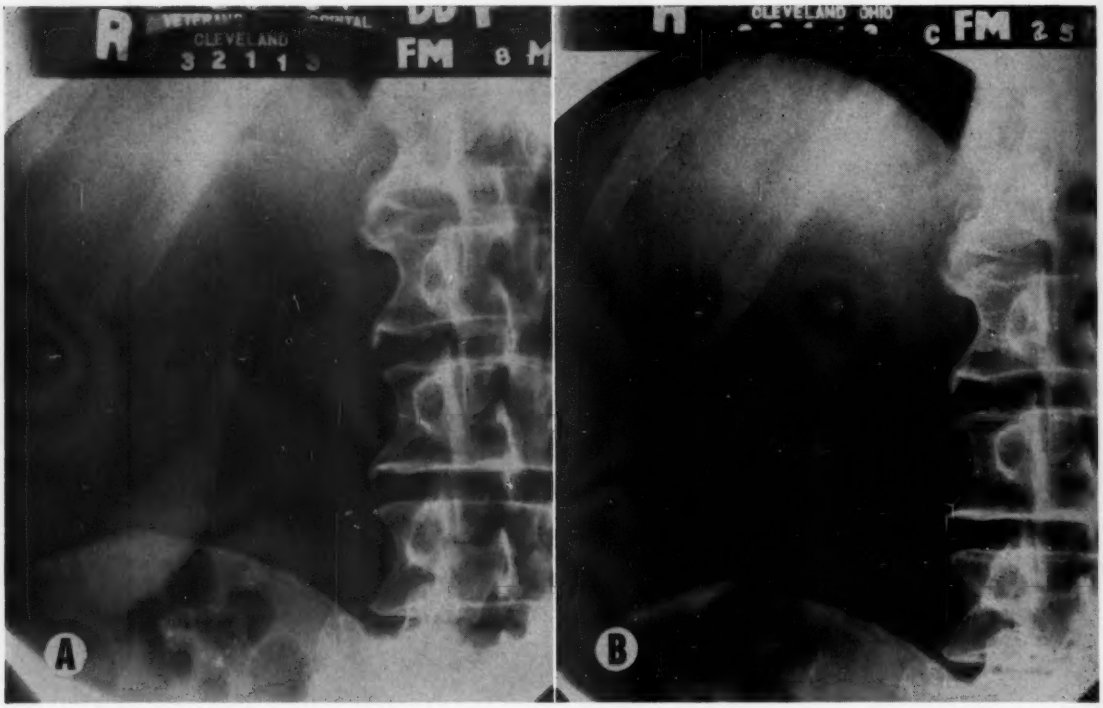


Fig. 8. Normal evacuation phase of the biliary tract. (*A* and *B*) C. R. T., eight and twenty-five minute films showing narrowing upper third of the gallbladder. Corkscrew or pearly appearance of a normal cystic duct. Common duct also normal.

With modern roentgenologic equipment, it is preferable to make exposures as rapidly as possible, *i.e.*, with a 500 ma. unit, rotating anode, fine focus tube. The factors Kerley recommends are favored: 75–80 kv., 400 ma. at 0.1 second, using a synchronized moving grid at 36 inch tube-target distance. With a 200 ma. unit, 150 to 200 ma. at 0.2 to 0.3 second can be used. In addition to the films being made as fast as possible, the patient's body should be immobilized with an abdominal binder, and a pressure device of balsam wood, inflated balloon or soft cotton is placed under the binder in the gallbladder area.

Films are taken in the prone left anterior oblique projection, 15 to 20 degrees, in order to better visualize the common duct, which frequently overlies the spine. Sometimes, immobilization and compression of the abdomen are facilitated if the film is made in a right posterior oblique projection. Upright and dorsal and ventral decubitus views are invaluable aids in the detection of calculi. Such views are not necessary in the study of the contractile phase of cholecystography.

ROENTGEN OBSERVATION OF GALLBLADDER EMPTYING

The findings of Bronner, and of Sussman and Copleman on visualization of the extrahepatic ducts were never universally accepted. In part, this may have been due to the economic impracticability of the procedure in a busy roentgen department. It is possible, as Copleman has reported, that the poor results of some of the recent investigators were due to the fact that priodax was used as the contrast medium. Priodax is a sympathicomimetic drug and retards gallbladder emptying.

Although the previous reports on visualization of the common duct and gallbladder evacuation were of value, it was believed that the common duct probably could be visualized more often if, in addition to serial films at short intervals, a drug with

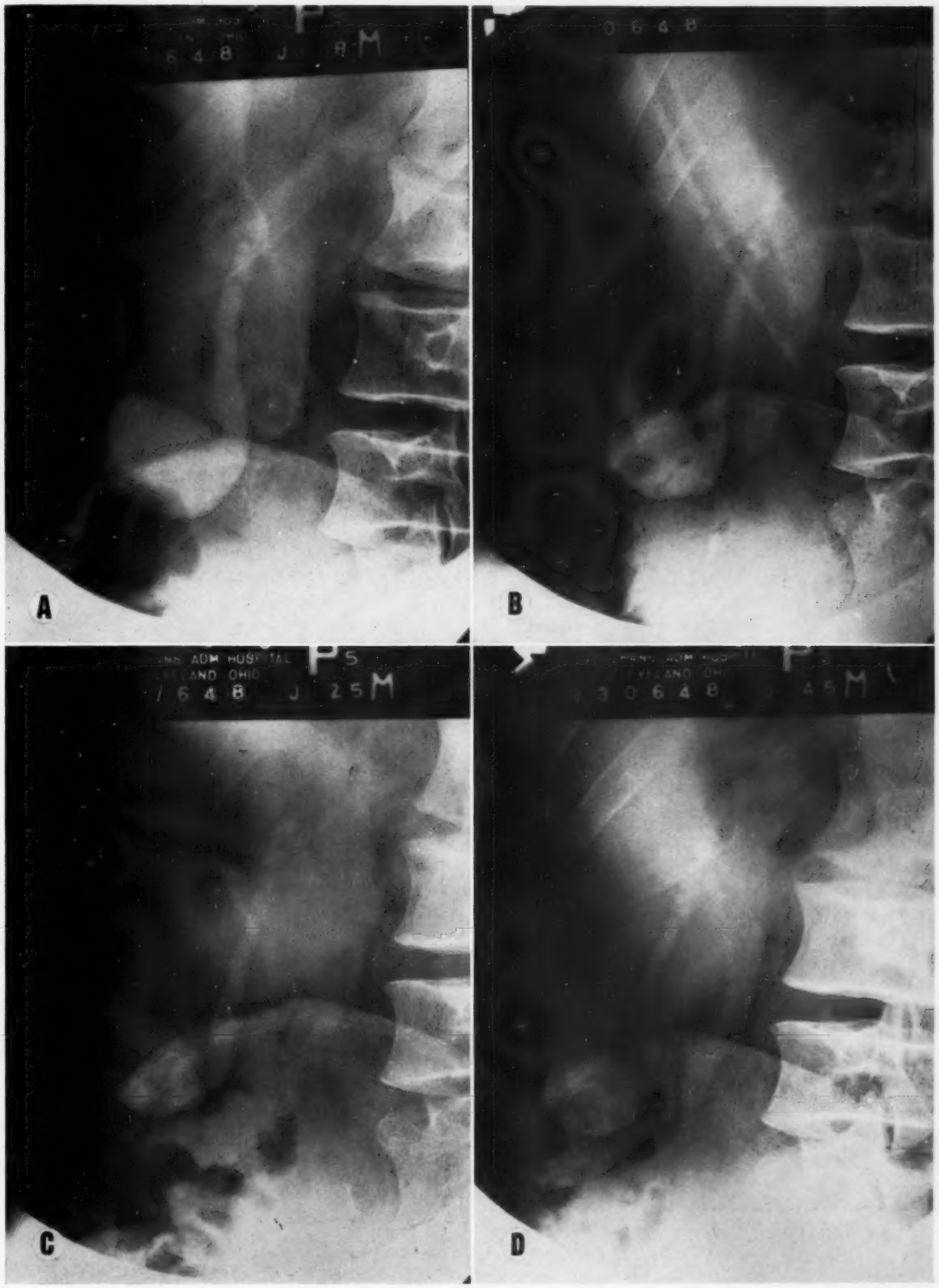


FIG. 9. Normal evacuation phase of Phrygian type gallbladder during a forty-five minute period. (*A*, *B*, *C*, and *D*) L. S., films taken after eight, fifteen, twenty-five and forty-five minutes. Note gradual contraction of upper half of gallbladder. Also pearly appearance of cystic duct and normal caliber of the common duct.

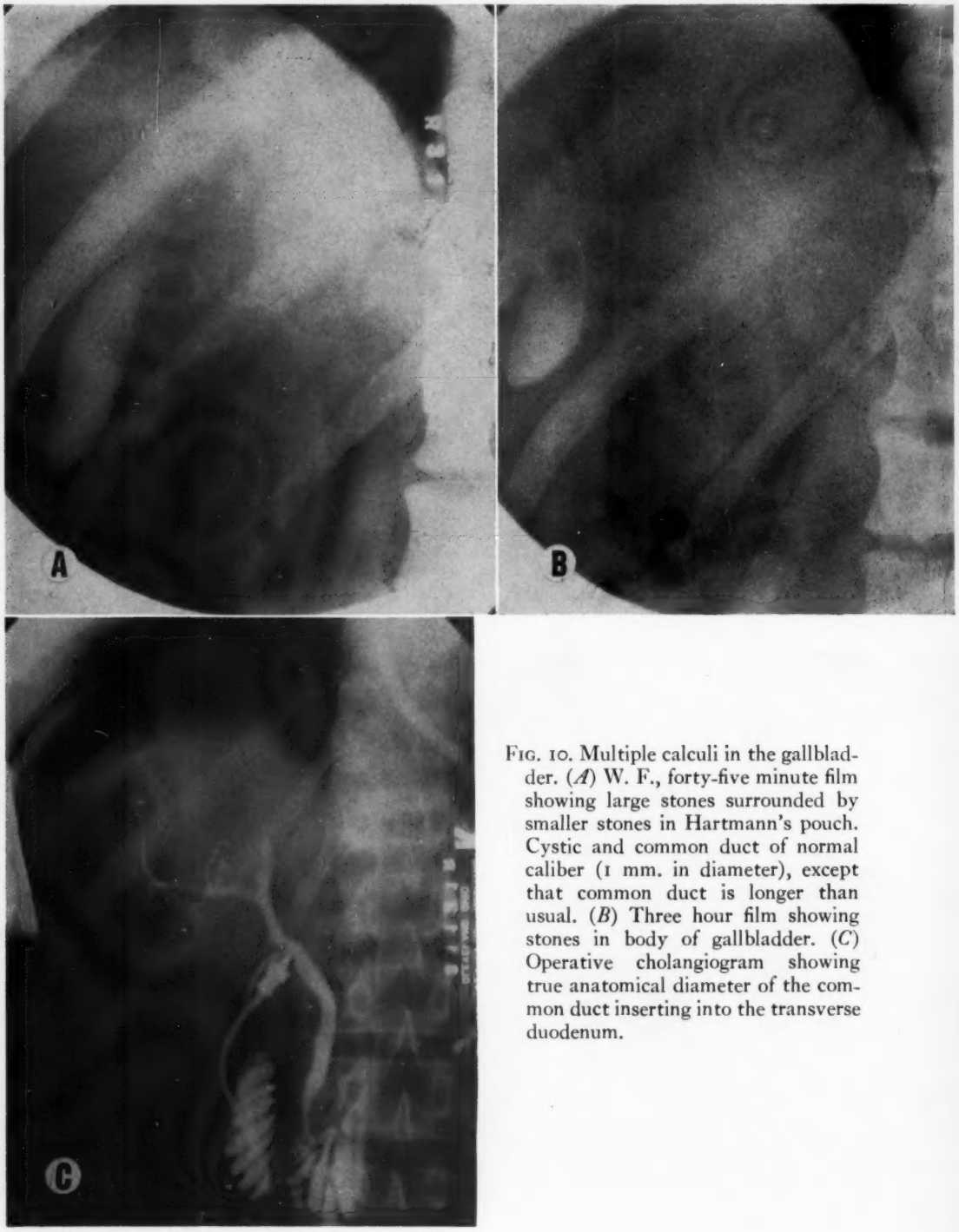


FIG. 10. Multiple calculi in the gallbladder. (*A*) W. F., forty-five minute film showing large stones surrounded by smaller stones in Hartmann's pouch. Cystic and common duct of normal caliber (1 mm. in diameter), except that common duct is longer than usual. (*B*) Three hour film showing stones in body of gallbladder. (*C*) Operative cholangiogram showing true anatomical diameter of the common duct inserting into the transverse duodenum.

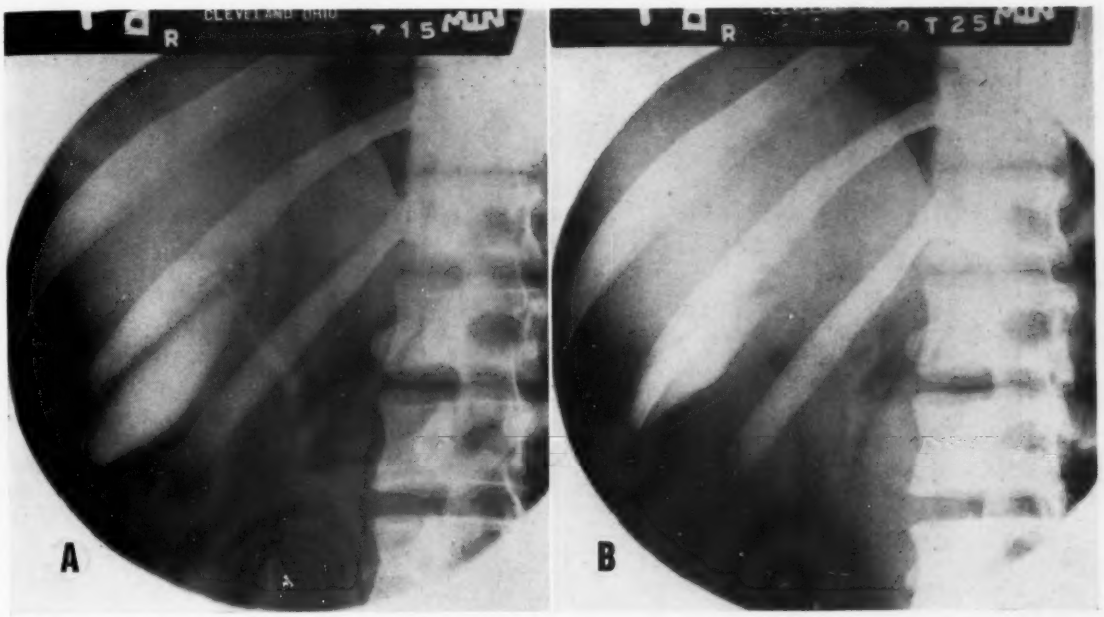


FIG. 11. Fifteen and twenty-five minute films showing obscuring of cystic duct which is looped on itself. (*A* and *B*) Normal common duct. Entire gallbladder somewhat contracted as a whole.

the property of constricting the sphincter of Oddi were given just prior to the fatty meal.

The obvious drug and first to be tried was morphine sulfate. Its action on the smooth muscles of the sphincter of Oddi and intestines was well known to physiologists and internists. A series of 89 patients was studied in which $\frac{1}{6}$ grain of morphine was given subcutaneously prior to the fatty meal. In no instance was either the cystic or common duct visualized. The density of the gallbladder was increased to such a degree that the roentgen technicians considered it as another good method for a better demonstration of a poorly visualized gallbladder.

The effect of morphine was not only to cause spasm of the sphincter of Oddi, but also to occlude the neck of the gallbladder at Lütken's sphincter (Fig. 5). For this reason, the gallbladder appears to have increased in density. At no time was contrast medium seen in the cystic duct and the gallbladder emptying time was delayed for over twenty-four hours (Fig. 6).

A number of vagoconstrictor drugs were then considered. From this list, prostigmine was selected. It is used extensively for postoperative distention and has an extremely low degree of toxicity. It not only raises the intestinal tone, which Ivy states is a contributing factor in biliary spasm, but also has a direct constrictive action on the smooth muscle of the sphincter of Oddi. There are no marked side reactions with prostigmine as with urocholin and other similar drugs.

Prostigmine is commonly used during cholecystography to expel intestinal gas. However, no cases have been reported in which the common duct was seen. This is probably due to the delay in time sequence of roentgen exposures following a fatty meal.

In the present study, the time interval for roentgenograms following a fatty meal in each case was judged empirically. In the majority of instances, the common duct was visible within eight to fifteen minutes. In a small percentage of cases, the ducts might have been seen at twenty-five minutes. Therefore, for the convenience of the radiologist and technician, automatic eight,

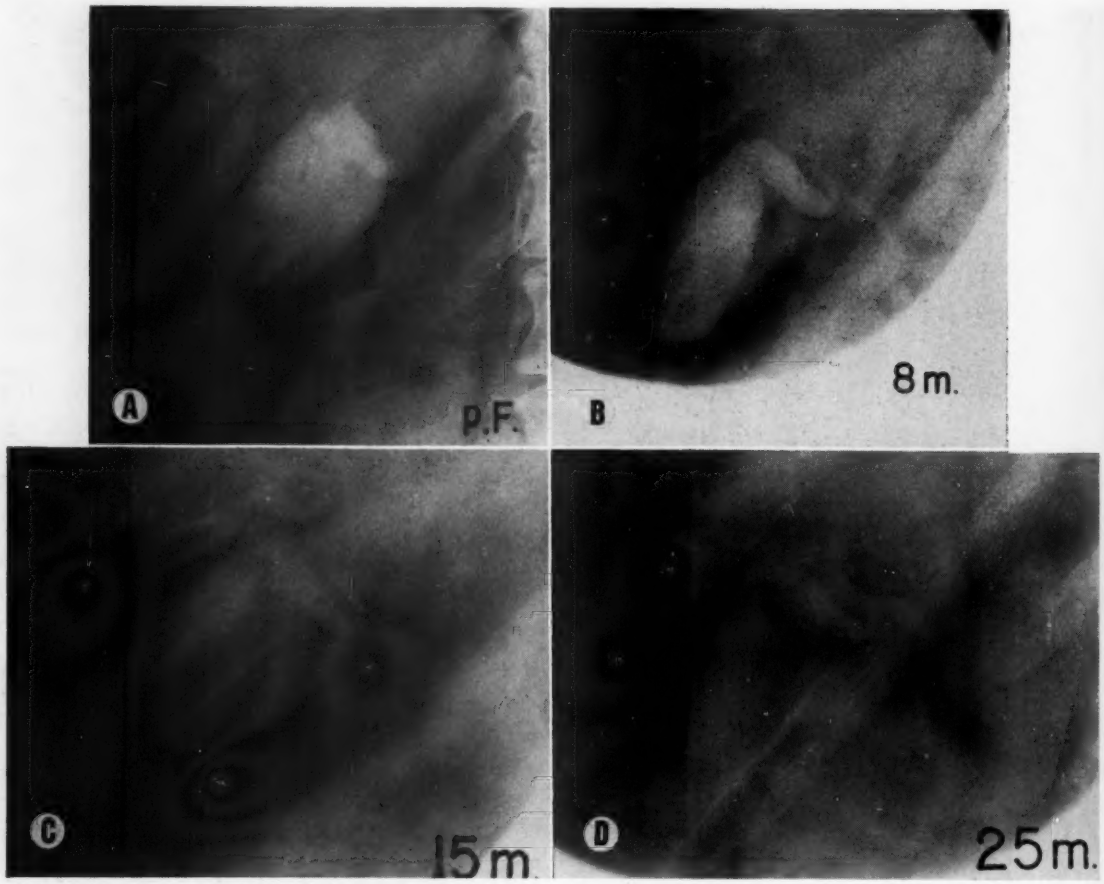


FIG. 12. Hypercontractibility of gallbladder in the presence of duodenal ulcer. (*A*, *B*, *C*, and *D*) M. S., a sixty-one year old white female with a five year history of a recurrent duodenal ulcer. Twenty-four hours prior to the last admission, the patient was nauseated and vomited continuously. Vomitus was white and thick. Gastrointestinal series revealed a deformed bulb which had not changed in appearance since the previous examination.

Note marked contractions and rapid emptying of the gallbladder. Cystic and common ducts are normal.

fifteen and twenty-five minute films were taken. These films provided an excellent study of the rate of evacuation, as well as a demonstration of the extrahepatic ducts. If, as occasionally occurred, the ducts were not seen, a forty-five minute film was taken. In all cases, three and six hour films were taken to study the degree of evacuation.

The pertinent roentgenoscopic findings were observed during the initial thirty minutes following the fat meal. Contractions began within eight minutes (Fig. 7). The gallbladder contracted as a whole or in segments, largely confined to the upper half. Multiple contractions made the gallbladder appear lobulated with the lobules arranged in a row, like a string of pearls. In some instances, the contractions were so complete that the upper half was contracted to the diameter of the cystic duct and appeared to be continuous with it (Fig. 8 and 9). True peristalsis was not observed. A gradual diminution in the size of the gallbladder was observed within the first twenty-five minutes. In most instances, the gallbladder was reduced approximately 25 to 50 per cent. If a forty-five minute and one-hour exposure were made, the reduction in size varied from 50 to 65 per cent. At three to six hours, the gallbladder was about 85 per cent its original size.

Fig. 13. Dysfunction (dyskinesia or spasm) of sphincter of Oddi in presence of a duodenal and prepyloric ulcer. A. G., a fifty-two year old male, with a nine year history of duodenal ulcer. Pain was relieved at night by milk. Gastrointestinal series revealed a duodenal crater as well as a prepyloric niche. Note narrowing of the sphincter of Oddi, proximal dilatation of the common duct and reflux into the common hepatic duct.

Heister's valves of the proximal half of the cystic duct resemble a corkscrew or a section of a string of pearls. The distal half of the cystic duct was smooth and was often difficult to differentiate from the common duct. The lumen of the cystic and common duct appeared equal in thickness and approximated the diameter of the lead of a lead pencil (1–2 mm.). Anatomically, the lumen of the common duct measures 7.5 mm. in diameter. However, roentgenographically, the smaller diameter of the column of contrast medium was due to the gallbladder contraction with the spurting of medium in a stream-like fashion through the duct (Fig. 10).

During the evacuation phase, the gallbladder sometimes obscures the cystic duct which may be coiled and looped over on itself (Fig. 11). No peristalsis has been observed in the extrabiliary tract. Sometimes, the common duct appears wavy, suggestive of peristalsis, but this is probably due to an elastic recoil mechanism.

This procedure may appear to require a great number of films, and thus to be uneconomical. If a compromise is necessary, a twelve-minute film can be substituted

Fig. 14. Prolonged spasm of the sphincter of Oddi in the presence of a duodenal ulcer. W. F., a sixty year old white male with an eight year history of duodenal ulcer proved roentgenographically. The gallbladder had been removed and the common duct explored three years before for acute cholecystitis with jaundice. There was recurrent right upper quadrant pain of three months' duration and jaundice for three days. Laboratory findings were consistent with obstructive jaundice. An operative cholangiogram shows a marked narrowing and irregularity in the region of the sphincter of Oddi with moderate dilatation of the proximal common and hepatic ducts, and the residual dilated cystic duct stump with medial insertion. No calculus is present. Postoperative cholangiogram six weeks later was normal. (From Cholangiography, Surgical Monograph, 75–149, 1951. Courtesy of Thomas Nelson & Sons, New York.)

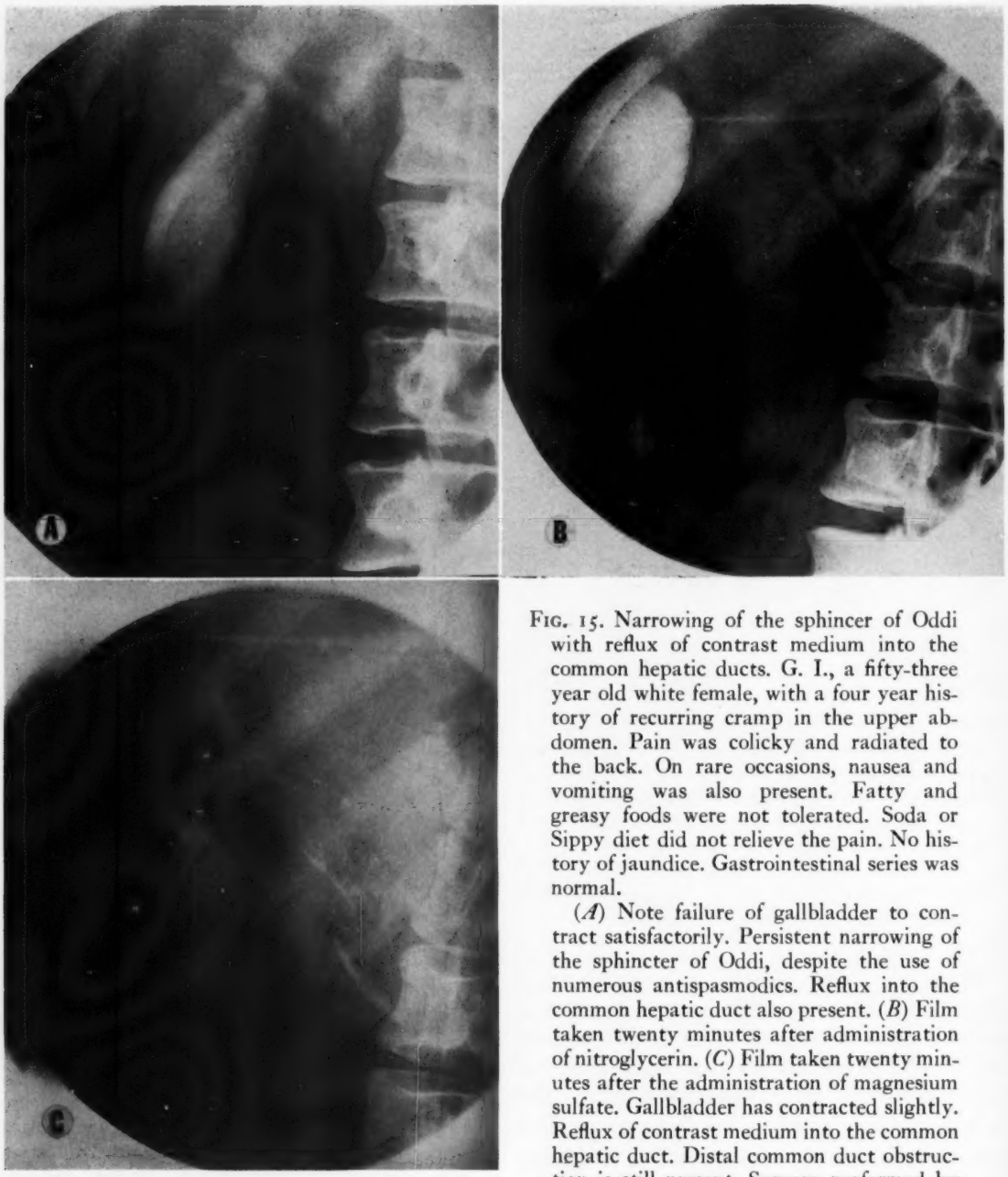


Fig. 15. Narrowing of the sphincer of Oddi with reflux of contrast medium into the common hepatic ducts. G. I., a fifty-three year old white female, with a four year history of recurring cramp in the upper abdomen. Pain was colicky and radiated to the back. On rare occasions, nausea and vomiting was also present. Fatty and greasy foods were not tolerated. Soda or Sippy diet did not relieve the pain. No history of jaundice. Gastrointestinal series was normal.

(*A*) Note failure of gallbladder to contract satisfactorily. Persistent narrowing of the sphincter of Oddi, despite the use of numerous antispasmodics. Reflux into the common hepatic duct also present. (*B*) Film taken twenty minutes after administration of nitroglycerin. (*C*) Film taken twenty minutes after the administration of magnesium sulfate. Gallbladder has contracted slightly. Reflux of contrast medium into the common hepatic duct. Distal common duct obstruction is still present. Surgery performed by Dr. Phillip Partington revealed a fibrosis of the sphincter of Oddi for which a sphincterotomy was done.

for the eight and fifteen minute ones. The twenty-five minute film is a good indicator of whether or not to take films other than a three hour one. However, as Kerley recently stated, it is the only method whereby the complete biliary cycle of filling, contracting and evacuating can be studied adequately in all its phases. In this manner a high degree of accuracy can be achieved, especially in cases of dysfunction of the sphincter of Oddi.

EVACUATION IN THE PRESENCE OF PEPTIC ULCER

According to the literature, in the presence of an ulcer, a normal visualized gallbladder was present in 85 per cent of the cases and a poorly visualized one in 15 per cent. Bronner reported that, in some ulcer patients, the evacuation time was unusually rapid, the gallbladder being completely empty within thirty-five minutes (Fig. 12). In the present study, the emptying time varied but was always somewhat short and associated with hyperactive contractions. Westphal's observations on vagus action seem to be confirmed roentgenographically. With marked ulcer activity, the sphincter of Oddi was in spasm, permitting the visualization not only of the common and cystic duct, but also of the common hepatic duct. Reflux into the common hepatic duct was not possible unless there was a distal obstruction, usually at the sphincter of Oddi, permitting an increased intraductal pressure (Fig. 13). It may be concluded, therefore, that in the presence of an ulcer, the gallbladder contractions are increased and spasm of the sphincter of Oddi may occur, possibly due to increased vagus activity (Fig. 14). Hyperacidity is undoubtedly a contributing factor toward the spasm, as shown by Doubilet and by Colp.

The close relationship of peptic ulcer to gallbladder disease has been mentioned by many authors; and these studies confirm the necessity of a gallbladder examination in the case of an ulcer which has not responded to a medical diet. From August, 1946, to May, 1950, 975 cases of duodenal ulcer were seen, of which 316 had cholecystography with 29 cases (9.1 per cent) of co-existing gallbladder involvement. From May, 1950, to August, 1951, there were 623 cases of duodenal ulcer. Of this number, 430 had cholecystograms with 86 instances (20 per cent) of gallbladder involvement.

If spasm of the distal common duct is allowed to persist, inflammation and even fibrosis may ensue (Fig. 15). In the presence of prolonged spasm or fibrosis, the proximal common duct becomes dilated (Fig. 16 and 17).

An antispasmodic can be given to determine how much of the narrowing of the sphincter of Oddi is due to spasm and how much to fibrosis. The most effective antispasmodic has been magnesium sulfate given through a duodenal tube. Banthine, because of its parasympathetic as well as sympathetic action, theoretically would seem to be ideal. Our experience is still too limited to permit us to make a statement concerning its effectiveness.

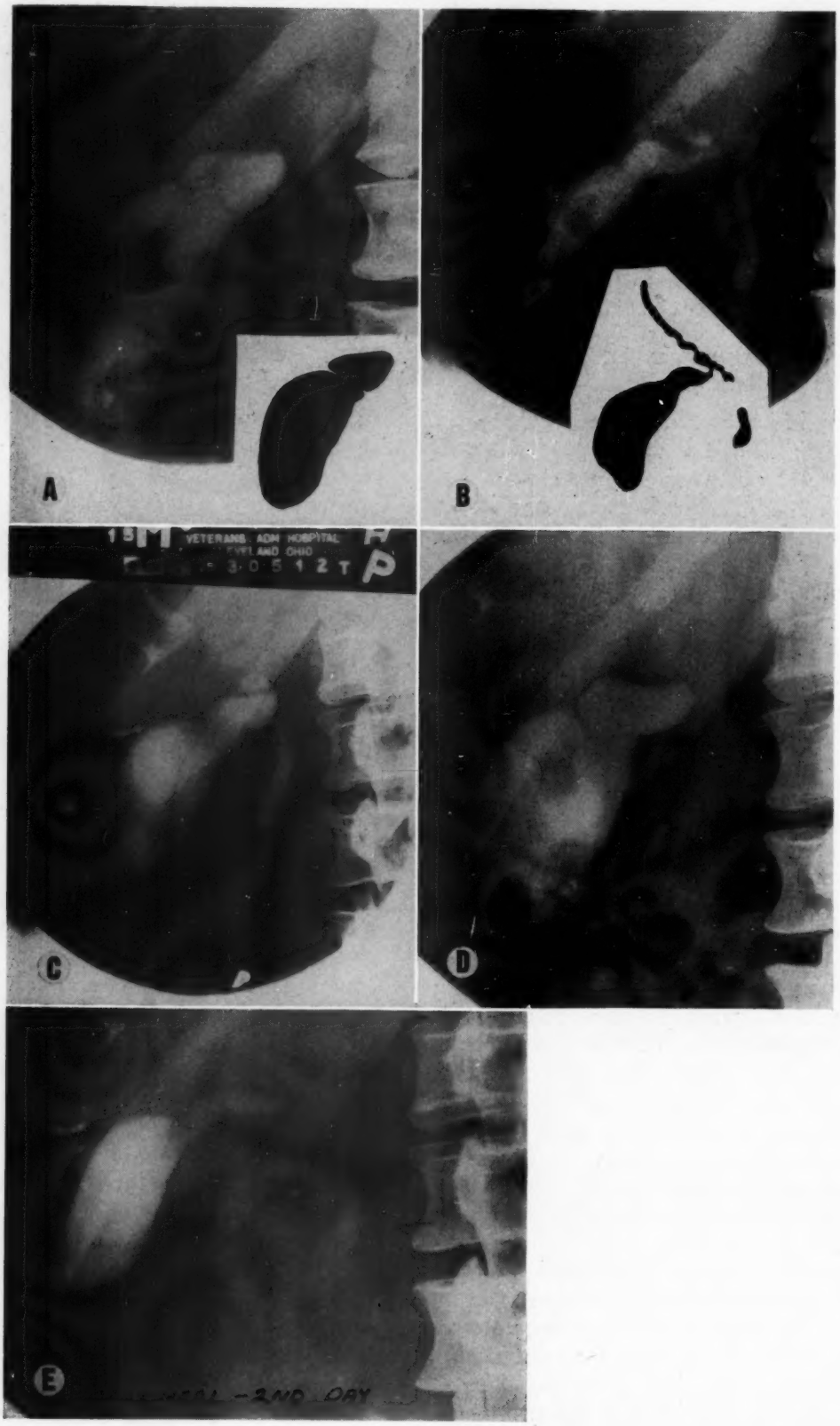
PANCREATITIS

In pancreatitis, the gallbladder may be distended, emptying is delayed and there is narrowing of the pancreatic segment of the common duct. This has been confirmed by cholangiography (Fig. 18, 19 and 20).

SUMMARY AND CONCLUSION

Up to the present time, pathological changes of the transduodenal segment of the common duct (sphincter of Oddi) have been diagnosed during an exploratory laparotomy, cholangiography, or at postmortem examination. Recent experience with evacuation studies during cholecystography in some instances confirmed by operative cholangiography has permitted the diagnosis to be made preoperatively thereby enabling the physician to plan the necessary proper medical or surgical therapy.

A thorough understanding of the pathological physiology of the biliary tract is essential. Cholecystography should consist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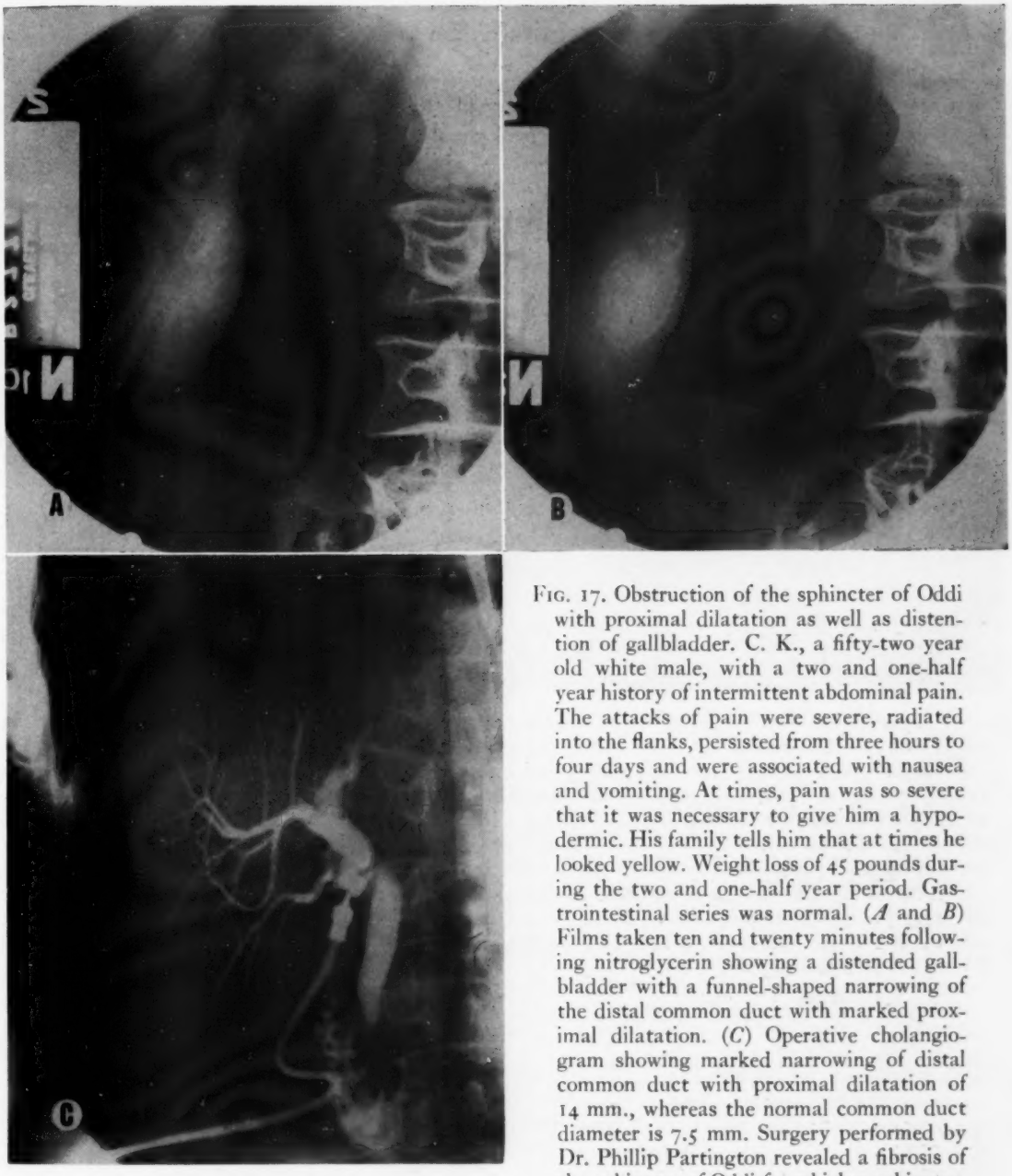

FIG. 17. Obstruction of the sphincter of Oddi with proximal dilatation as well as distention of gallbladder. C. K., a fifty-two year old white male, with a two and one-half year history of intermittent abdominal pain. The attacks of pain were severe, radiated into the flanks, persisted from three hours to four days and were associated with nausea and vomiting. At times, pain was so severe that it was necessary to give him a hypodermic. His family tells him that at times he looked yellow. Weight loss of 45 pounds during the two and one-half year period. Gastrointestinal series was normal. (*A* and *B*) Films taken ten and twenty minutes following nitroglycerin showing a distended gallbladder with a funnel-shaped narrowing of the distal common duct with marked proximal dilatation. (*C*) Operative cholangiogram showing marked narrowing of distal common duct with proximal dilatation of 14 mm., whereas the normal common duct diameter is 7.5 mm. Surgery performed by Dr. Phillip Partington revealed a fibrosis of the sphincter of Oddi for which a sphincterotomy was done.

FIG. 16. Obstruction of the sphincter of Oddi with reflux into the common hepatic duct. R. L., a fifty-seven year old male, with a six year history of indigestion. Pain was gnawing and relieved by food. One year prior to the hospital admission, a tarry stool was noted. Gastrointestinal series revealed a duodenal ulcer for which he was treated with relief of symptoms. He returned to the hospital one year later with a recurrence of his symptoms. He also complained of belching and pain in the left flank. Appetite was poor and he has lost 35 pounds in weight. (*A*) Examination January, 1951. Pre-fatty meal film showing distended gallbladder with Hartmann's pouch. (*B*) Fifteen minute post-fatty meal film showing obstruction of distal common duct with proximal dilatation. (*C*) Examination August 14, 1951. (Duodenal ulcer still present.) Funnel-shaped obstruction of distal common duct present with suggestive concave defect. Reflux in common hepatic duct present. (*D*) Re-examination August 17, 1951. Forty minutes after the administration of morphine. Common duct is not demonstrable and gallbladder is somewhat distended. (*E*) Gallbladder has contracted slightly, especially in the upper third, but the obstruction of the distal common duct with proximal dilatation is still present.

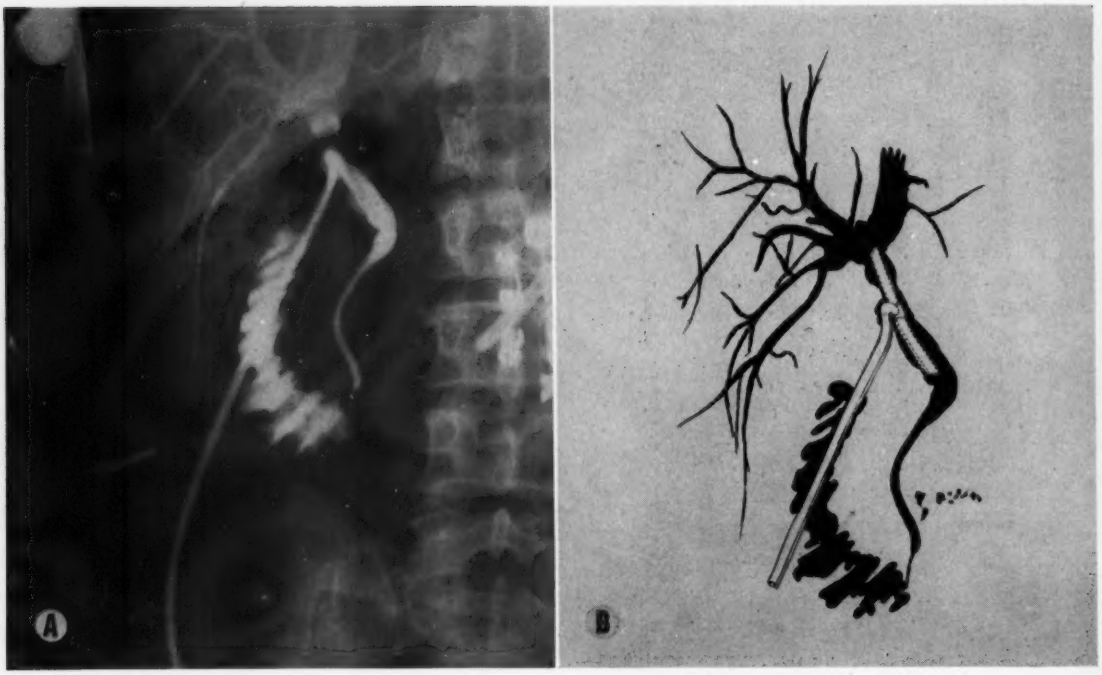

FIG. 18. Pancreatitis with narrowing and displacement of the common duct. C. J., a forty-three year old white male, a chronic alcoholic, with a three week history of sharp epigastric and right upper quadrant pain radiating to the back. There was a firm, tender, somewhat irregular mass in the right upper abdomen extending down to the umbilicus. The cholecystogram revealed a functioning gallbladder. At laparotomy there were enlargement and induration of the head of the pancreas with a small pseudocyst arising from the superior border of the body of the pancreas. An operative cholangiogram through a T-tube shows marked narrowing and displacement of the pancreatic segment of the common duct. There is persistent narrowing of the transduodenal segment. The proximal common duct and hepatic branches are slightly dilated. Note the calcareous deposits in the head of the pancreas and the insertion of the common ducts into the transverse duodenum. (From Cholangiography, Surgical Monograph, 75–149, 1951. Courtesy of Thomas Nelson & Sons, New York.)

FIG. 19. Pancreatitis with narrowing, angulation and displacement of the common duct. P. S., a thirty-four year old white male, with a three year history of recurrent jaundice and mild transitory right upper quadrant pain which had been diagnosed as infectious hepatitis on two previous hospital admissions. The cholecystogram revealed a functioning gallbladder with possible nonopaque calculi. The liver chemistry was consistent with obstructive jaundice. An operative cholangiogram shows narrowing and displacement of the pancreatic segment of the common duct. Small calculi are present in the supraduodenal segment with proximal dilatation of the biliary tract. (From Cholangiography, Surgical Monograph, 75–149, 1951. Courtesy of Thomas Nelson & Sons, New York.)

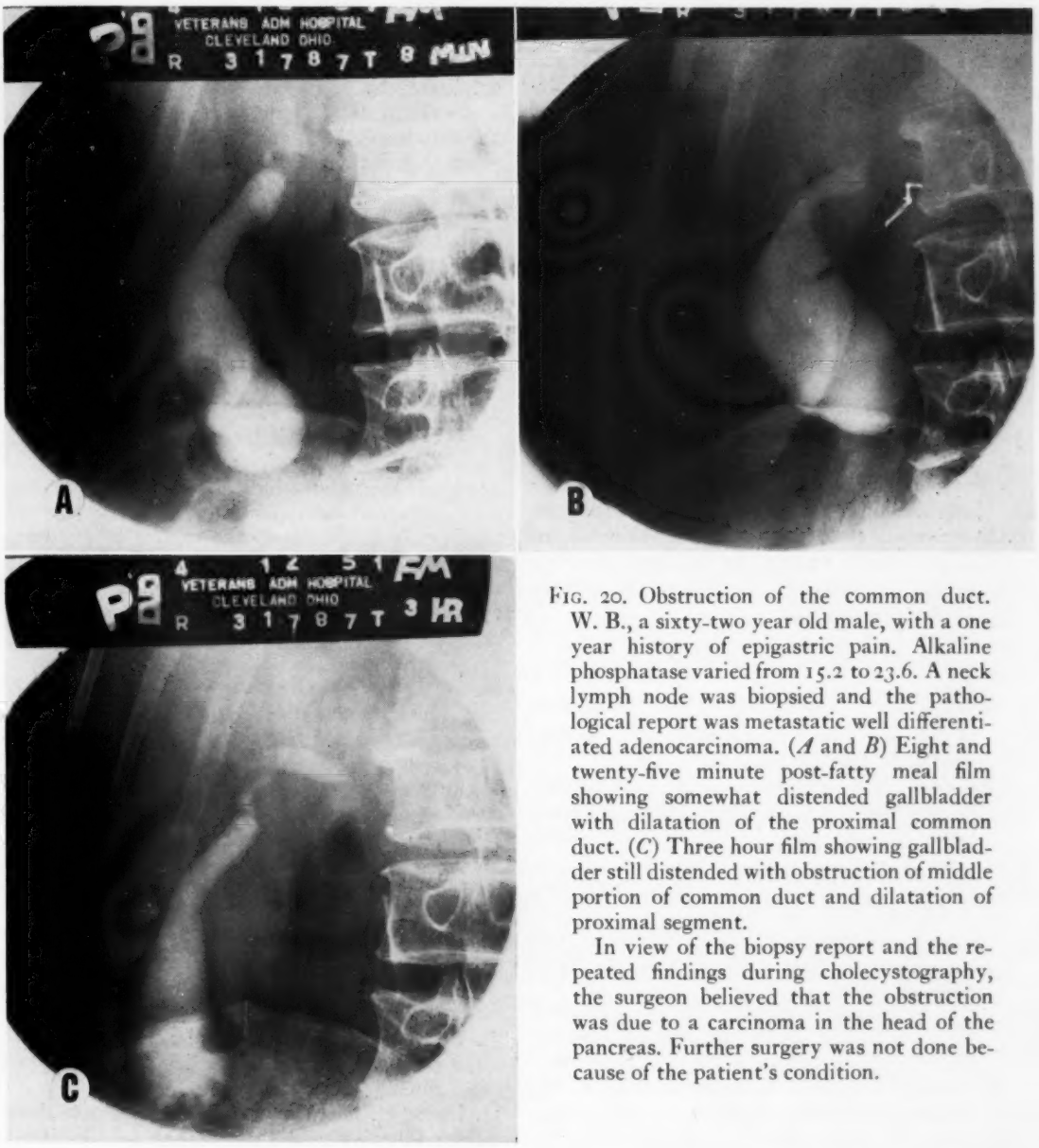

FIG. 20. Obstruction of the common duct. W. B., a sixty-two year old male, with a one year history of epigastric pain. Alkaline phosphatase varied from 15.2 to 23.6. A neck lymph node was biopsied and the pathological report was metastatic well differentiated adenocarcinoma. (*A* and *B*) Eight and twenty-five minute post-fatty meal film showing somewhat distended gallbladder with dilatation of the proximal common duct. (*C*) Three hour film showing gallbladder still distended with obstruction of middle portion of common duct and dilatation of proximal segment.

In view of the biopsy report and the repeated findings during cholecystography, the surgeon believed that the obstruction was due to a carcinoma in the head of the pancreas. Further surgery was not done because of the patient's condition.

of multiple films taken at approximately eight minute intervals during the first thirty minutes following the fatty meal. Additional films, at varying time intervals as determined by the roentgenologist, should be taken if there is evidence of abnormal biliary function. In conjunction with this technique, prostigmine, by its action on the sphincter of Oddi, aids in the visualization of the common duct. Only in this manner can such findings as dysfunction or fibrosis of the sphincter of Oddi or compression of the common duct by pancreatitis be diagnosed by cholecystography.

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DISCUSSION

Dr. Paul C. Swenson, Philadelphia, Penna. Dr. Sachs has given us an interesting discussion of the physiology of the gallbladder and we should be indebted to him for his presentation. His paper serves to strengthen the impression that whenever the surgeon takes out a gallbladder which is visualized and has no apparent stones, he is asking for trouble if he has not considered other complicating factors. Any gallbladder which is visualized, in most cases falls into the realm of medical treatment, even though it may be functionally deranged to some degree. At least the surgeon should probably look elsewhere for the difficulty, as Dr. Sachs has shown.

At Jefferson Hospital, we have been working on some of the problems of gallbladder function in cooperation with our Department of Physiology. Among other things we have recently compared the cholecystogram with the secretin test and have found that we can sometimes use the latter to increase our accuracy of diagnosis. The cholecystogram, however, is by far the simpler of the two. We have also been studying the emptying of the human gallbladder under the stimulus of insulin administration. When a hypoglycemia is produced, there is an indirect excitation of the vagus. This is evidenced by the increased gastric motility as well as increased gastric and pancreatic secretions. There is, however, no evidence of gallbladder evacuation if precautions are taken to exclude the entrance of acid into the intestine or if the subjects are achlorhydric patients. The implication of this finding is that in man the effect of vagus stimulation on the gallbladder is minimal and that it is probably the cholecystokinin mechanism which is important in regulating evacuation. Unquestionably, contraction of the sphincter of Oddi will prevent gallbladder evacuation. However, Snape, Thomas and Friedman are of the opinion that the sphincter of Oddi functions mainly as a mechanism to prevent reflux of duodenal contents into the biliary tree, rather than to regulate the flow of bile into the duodenum. This view is consistent with the role of most all of the sphincters in the body economy.

We would therefore like to raise this question: Can the condition we clinically call biliary dyskinesia be of enteric rather than biliary origin? In other words, we question the very existence of this syndrome; *i.e.*, imbalance between the gallbladder and the sphincter of Oddi.

I am sorry Dr. Copleman, who was here earlier this week, could not remain to add to

this discussion, since he with Dr. Sussman has been quoted in this paper. These authors were able to show the duct system without the aid of drugs. They called attention to the fairly frequent reflux of the opaque material into the hepatic branches, never satisfactorily explained. Dr. Copleman gave me to understand that he had given up any attempt to routinely visualize the ducts, because he felt it had no immediate practical application. Particularly is this true if priodax is the opaque material employed.

I question the feasibility of taking so many films as a routine measure. Dr. Sachs makes the remark that the findings of Bronner, and Sussman and Copleman on the visualization of the extrahepatic duct system was never universally accepted. He points out that this may be in part due to the economic impractibility of the procedure in a busy roentgen department, and I am inclined to agree with him, unless by his new routine he shows us a much greater specificity of findings than his films seem to show. His use of prostigmine to enhance the image of the duct system is very interesting provided he can make real use of his findings. I note that one case in which he showed the narrowing of the common duct due to fibrosis of the pancreas was demonstrated by operative cholangiograms only. To me the findings are not very convincing on the plain roentgenograms.

One might ask why it is necessary for Dr. Sachs to give any drugs at all when one can gain the same end without them. If one is trying to demonstrate disordered function, is one not, by the drugs, creating an abnormal state which will not reflect the true picture; and again is not one taking a chance of producing a great deal of discomfort to the patient and perhaps precipitating colicky pain? Also, would one dare to advise a surgeon to do a sphincterotomy on any findings which have been demonstrated roentgenographically? I would consider the cholangiogram of the case, on which a sphincterotomy was done to be relatively normal with the exception of mild dilatation. Has Dr. Sachs actually been able to make a definitive diagnosis by the new routine which would point toward surgical intervention? If not, then for practical purposes, I think it would be poor economy to do this special procedure with the only object in view of gaining some knowledge of dysfunction, for the treatment in any event would be a trial and error proposition.

In discussing the physiology, Dr. Sachs points out that there is no evidence of peristalsis in the common duct. This I believe is a statement which would not coincide with many statements in the literature to the contrary both in humans and in laboratory animals. In fact, I believe I have observed it under roentgenoscopy when doing a cholangiogram without the tube within the duct. The opaque material was injected through a fistula.

It is unfortunate that the greatest indication for visualization of the extrahepatic duct system usually precludes the desired result, namely, the visualization of common duct stones, or, very rarely, a filling defect. Because of the obstructive manifestations this has never been done to my knowledge.

I therefore think that the routine which Dr. Sachs suggests might be reserved for the rare case where a normal cholecystogram is being re-checked because of a confusing clinical background, but doing it routinely as far as my department is concerned would be difficult. I am not thinking of the economy of films so much as that of time and what is eventually gained thereby. When the gallbladder is visualized, however, we can all point to the work of Dr. Sachs and others as emphasizing that the indications for cholecystectomy then are few.

DR. WILLIAM H. SHEHADI, New York, New York. I want to thank Dr. Sachs for a very stimulating presentation. The material given is worthy of considerable serious thought. His opening remarks are most timely and appropriate. They certainly reflect problems with which we as radiologists are constantly being confronted, and which invite discussions of varying intensity with our surgical colleagues.

The visualization of the entire biliary tract—not only the gallbladder—has been the dream of radiologists; visualization of the gallbladder and all the biliary radicles in exactly the same manner in which we can visualize the urinary tract. It has been my privilege recently to utilize a drug as a cholecystographic medium that is not yet on the market but will be available soon. I am sure that there are many in this audience who have had the opportunity to test it. It is known as Telepaque. In my observations, a very high incidence of visualization of the ducts has occurred without the administration of morphine or other drugs, such as Dr. Sachs has utilized.

Our observations have demonstrated that the normal extrahepatic ducts, contrary to

what we expected them to be from operative cholangiography and examination of the anatomical specimen, is approximately 1 to 2 mm., as Dr. Sachs has estimated. During the course of our investigation, which included over 300 cases, we have been able to visualize a number of cases where there was dilatation of the ducts —dilatation of the common, dilatation of the common and cystic, dilatation of the common, cystic and hepatic with reflux into the duodenum. The narrow portion of the sphincter of Oddi is apparent in exactly the same manner in which Dr. Sachs has demonstrated it.

I do not know whether I am in a position or whether we are in a position to fully evaluate these findings, and the observations that have been made at this time. Perhaps in a year or so we will be having reports of more observations on visualization of the ducts with or without the additional administration of medication. At that time more adequate evaluation may be possible. I fully agree with Dr. Sachs that we have two conditions which clinically go under the syndrome of so-called gallbladder disease, but we have a great deal more to learn about the ducts whether we use artificial medication such as Dr. Sachs has done or whether we are able to visualize the ducts otherwise.

I want to thank Dr. Sachs again for his stimulating paper and I appreciate the opportunity of presenting these remarks.

Dr. Sachs (closing). I would like to take this opportunity to thank both discussants for their remarks and observations on cholecystography. Dr. Swenson raises the question whether such a syndrome as biliary dyskinesia (that is, imbalance between the gallbladder and the sphincter of Oddi) actually exists. Certainly, most of the authorities in the field of physiology believe that there is such a syndrome. Many authorities believe that an imbalance does exist between the gallbladder and the sphincter of Oddi; others believe that it may be partially of an enteric origin. Undoubtedly, there is a delicate mechanism, to some extent controlled by the autonomic nervous system, regulating the balance existing between the gallbladder, sphincter of Oddi and the gastrointestinal tract.

In a letter to me, dated January 10, 1951, Dr. Copleman made the following statement:

> Our studies were hampered by the fact that priodax did not lend itself to these investigations as nicely as did the tetraiodophenolphthalein. I had found that for some reason, perhaps inherent in the size of the dose I had used (5 to 7 gr.), emptying was considerably delayed. Only in the occasional case was there complete emptying such as we used to see with the tetraiodo salt.
>
> My impression has always been that in visualization of the common hepatic duct, and even more so with visualization of the smaller radicles, hypertonicity of the sphincter of Oddi was present. I have never been successful in reproducing this reflux on an otherwise normal patient with the aid of drugs. On the other hand, patients who showed the reflux, which I believe is evidence of biliary dyskinesia, demonstrated the same phenomenon on subsequent examinations.

Our experiences have been similar to those of Dr. Copleman. Priodax causes a definite retardation in evacuation and the percentage of successful visualizations of the common duct is no higher than between 20 and 25 per cent; however, with the use of prostigmine, the common duct can be seen in about 75 per cent of the cases. The action of prostigmine is of short duration and does not produce colicky pain or undue discomfort. It has been in universal use to displace gas during urography and cholecystography and for postoperative distention.

The operative cholangiogram to which Dr. Swenson refers shows definite dilatation of the proximal common duct, visualization of the entire intrahepatic radicles, as well as narrowing of the sphincter of Oddi segment. Increase in back pressure to such an extent that the intrahepatic tree is visualized is, in our experience, indicative of persistent involvement and one that has existed for some time. Subsequently, the roentgen interpretation of obstructive narrowing of the sphincter of Oddi was proved at surgery. The surgeon was only able to pass a No. 6 urethral catheter through the obstruction of the sphincter of Oddi. Therefore, through a duodenal approach, the sphincter of Oddi was cut and sections through the wall at this point showed increased thickness due to fibrosis. Dr. Swenson quotes this case as being due to fibrosis of the pancreas. Apparently he misunderstood my original statement for his quotation is incorrect: the fibrosis involved the sphincter of Oddi, not the pancreas. In our experience with routine operative cholangiography during the past six years, we have found that a common duct with a transverse diameter above a maximum of 11 mm., together with visualization of the intrahepatic

radicles, had been caused by an obstruction of the distal segment of the common duct.

It is possible that the "peristalsis" which Dr. Swenson states he has observed during roentgenoscopy may not have been a true peristaltic wave but actually a mechanical distention of the duct due to the contrast medium injected under a definite pressure. As the medium flows onward, there is a relaxation of the pressure and the wall of the common duct rebounds to normal.

This method of cholecystography should be a routine one, not merely reserved for special instances. Would it not be difficult to determine which so-called "normal cholecystogram" should be rechecked? However, for practical purposes, the procedure may be modified, depending upon the department and its adaptability: for example, one film may be taken at twelve minutes and a second, at twenty-five minutes, instead of the eight, fifteen and twenty-five minute films. In the majority of cases, it is not necessary to take a three and six hour film. In this study of gallbladder evacuation, for the sake of thoroughness, three and six hour studies were done.

If this procedure is carried out routinely, further knowledge will be acquired concerning so-called dysfunction or dyskinesia of the sphincter of Oddi. In this manner, the cholecystographic examination will be of considerable help to our medical and surgical colleagues

HEMANGIO-ENDOTHELIOMA OF THE PELVIS

FOLLOW-UP OF PREVIOUSLY REPORTED CASE

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IN THIS JOURNAL, in April, 1950, we reported a case of hemangio-endothelioma of the pelvis with a twelve year radiation response.[1] Due to the apparent interest reflected by the many requests for reprints, we feel it would be most valuable to record the subsequent progress and postmortem findings fifteen years later in this rare and unusual case.

CASE REPORT

For more extensive details of this case we refer to our original article; however, the events which have led to this second paper date back to April 3, 1936. Briefly, the following is given to help acquaint the reader with the essential results:

Mrs. I. M., then aged twenty-eight, was first seen at St. Luke's Hospital in Kansas City, Missouri. She complained of abdominal pain originating in the epigastrium, radiating to the right lower quadrant. At this admission, an indefinite mass was noted on the left side extending from the anterior iliac crest to the midline of the abdomen. The uterus was "frozen," with thickening of the broad ligaments. At surgery, a large irregular mass was readily evident, distorting the left broad ligament and overlying the sigmoid colon. The pathological report by Dr. Ferdinand Helwig‡ was hemangio-endothelioma of the broad ligaments.

Two months later there was recurrence of the abdominal pain which was so severe it necessitated a second operative investigation.

The pelvic organs at this time were distorted with cystic vascular areas. Due to the obvious futility of any surgical intervention, a biopsy was taken and the patient referred to the Tumor Clinic at Menorah Hospital where it was decided to give radiation therapy. Thus a roentgen cycle to the pelvis was started on November 23, 1936.§

The patient was observed for several years following this roentgen therapy and did not return to the clinic until November 8, 1948, an interval of eleven years. On this admission, she complained of recurrence of pain of moderate severity. Examination revealed a somewhat movable uterus, normal in size. The right parametrium was pliable but there was induration on the left extending a few centimeters out laterally in the broad ligament. This area was extremely tender to palpation. In view of these findings another pelvic cycle was given.

She was then seen at six month intervals until her final admission to St. Luke's Hospital on August 13, 1951.

At this time there was a history of cramping abdominal pain accompanied by vomiting. The patient had vomited a large quantity of black-brown material possessing a strong fecal odor. The patient was taken to the operating room for an emergency exploratory operation.

At surgery there was no evidence of local obstruction, but instead there were zones of hemorrhagic bowel with marked edema and the patient died shortly after the surgical intervention.

Gross study limited to the abdominal cavity revealed areas of small intestine distended with gas and fluid. In addition, there were three zones, 2 cm. wide, which were dark brown in color. These corresponded to the region in which the mesenteric vessels were filled with blood clot. In the root of the mesentery there was a large hard mass measuring 8 by 3 by 4 cm., lobular in appearance and whitish in color. In addition, there were several enlarged hard lymph nodes in the mesentery and the abdominal surface of the right diaphragm was covered by several hard nodules up to 25 mm. in diameter, but the left diaphragm was normal. The pelvis, which had previously been irradiated, was uninvolved.

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§ Details of treatment in original article.

The histopathologic study of the tumor revealed a diffuse hyaline fibrosis with occasional little vascular spaces scattered throughout. There were wide areas of collagen replacing the tumor and small nests of oval and spindle cells attempting to form tiny vascular channels.

Impression: Hemangio-endothelioma of the pelvis (treated fifteen years ago) with metastasis to the right diaphragm and mesenteric glands, thrombosis of the terminal branches of the mesentery artery with gangrene of the small intestine, extensive sclerosing and collagenous changes which had taken place in recurrent areas.*

SUMMARY

1. Our purpose in this follow-up report is to record the subsequent progress and postmortem findings in a case of hemangio-endothelioma of the pelvis.

2. This patient, treated by roentgen therapy over the pelvic area, survived fifteen years and at postmortem examination there was no evidence of the tumor within the area treated.

3. Recurrence of the hemangio-endothelioma was evident in mesenteric glands at the root of the mesentery and under the right diaphragm.

CONCLUSION

1. Individual case reports of this rare condition should add to our knowledge concerning its treatment.

2. Hemangio-endothelioma of the pelvis is radiosensitive.

3. Irradiation over the entire abdomen is suggested in view of the recurrence of this tumor in the regions of the mesentery and the right diaphragm.

David S. Dann, M.D.
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REFERENCE

1. RUBIN, S., and DANN, D. S. Hemangio-endothelioma of pelvis. AM. J. ROENTGENOL. & RAD. THERAPY, 1950, *63*, 545–547.

* In review of the literature preparatory to reporting the above case in the April, 1950, issue of this JOURNAL, we overlooked 3 cases of hemangio-endothelioma of the uterine cervix treated with radium by Bowing, Fricke and McClellan. (Bowing, H. H., Fricke, R. E., and McClellan, J. T. Radium therapy of hemangio-endothelioma of the uterine cervix. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 653–658.)

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DISSECTION OF THE NECK AFTER INTENSIVE IRRADIATION TO THE NECK

ITS FEASIBILITY IN THE MANAGEMENT OF CERVICAL METASTASIS FROM ORAL CANCER*

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IN THE minds of some, the approach to the management of cervical lymph node metastasis from oral cancer is a settled or quasi-settled problem. But a review of modern literature reflects the existing diversity of opinion and the uncertainty which exists in the minds of those apparently best qualified to judge. In some instances, one notes powerful surgical bias at work; in other instances, equally strong radiologic prepossession seems in control.

It is the purpose of this paper to describe a technique which, although not original, certainly is uncommonly employed and to evaluate the feasibility of this approach from a technical standpoint. It is not the purpose of this communication to evaluate whether or not this technique is superior to other methods.

Many surgeons and radiologists have believed that radical neck dissection is not a technically feasible procedure following intensive roentgen irradiation to the neck.[45,76,80,95,118] It has been believed that after intensive irradiation extensive operations are technically exceedingly difficult, if not impossible, to perform, and, if performed, the risk of serious complications is great.[45,76,80,111] No doubt, in consequence of this belief, a patient with oral malignancy presenting cervical metastasis at the time radiation treatment is started to the primary lesion is today nearly always treated as a purely radiological problem. That is to say, the metastatic disease is managed entirely from beginning to end by some combination of irradiation. This purely irradiation technique has been adhered to in the past even by those who believe strongly that radical neck dissection is the method of choice if metastasis develops any time *after* control of the primary lesion.

It appears illogical to follow the belief that neck dissection is the method of choice if the metastasis develops after control of the primary lesion and, at the same time, adhere to the conviction that irradiation techniques are to be preferred if the metastasis is present at the outset of treatment. If radical neck dissection is so desirable, when performed on later developing metastasis, what makes it so undesirable a method of management if metastasis is present in the beginning? It appears that the only reason for the above view would be that radical surgery is regarded as a technically nonfeasible procedure after intensive irradiation. It must be true that, in the minds of many, indeed most, workers who treat oral malignancy, radical surgical procedures on the neck, such as radical neck dissection, are considered to be technically impossible without undue operative risk, if attempted after intensive roentgen therapy. Any other reason for these apparently divergent views in one mind escapes us.

The employment of irradiation prior to surgery is not a new idea. For many years small amounts of radiation (1 or 2 threshold erythema doses to the entire lateral neck) were delivered either before or after operation by various men in the hope that some benefit would accrue (Fig. 1). This method

* Presented in a Symposium on the Head and Neck at the Thirty-third Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–9, 1951.

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of treatment was gradually abandoned during the 1930s as evidence accumulated which strongly suggested the doubtful value of this technique. Nonetheless if this experience accomplished nothing else, it showed that a dose of 2,000 roentgens (measured in air) to a field 10 by 15 cm. in fractionated doses of fairly high quality radiation (180–200 kv., peak) was not incompatible with normal wound healing.[59]

Some workers, appreciating the doubtful value of such low doses of radiation, gave more intensive irradiation prior to and following surgery.[20,48,49] Several papers written by authors apparently having experience with patients subjected to intensive irradiation to the neck, followed by radical surgery, condemn the practice.[45,76,93,95,113] In view of this strong condemnation, neck dissection after intensive irradiation to cervical metastasis fell into disrepute. A most notable exception to the general condemnation stands out. The exception is the late Engelstad of Norway. His contributions of 1938 and 1945 are the only ones known to the authors which undertake an analysis of preoperative irradiation followed by neck dissection before stating his conclusions.[48,49] Engelstad in 1938 and 1945 recommended preoperative irradiation (teleradium) followed by radical neck dissection. A contribution by Weyde,[129] apparently working in the same clinic and following the same technique as laid down by Engelstad, agrees with his conclusions.

FIG. 1. The dotted lines indicate the operative extent of the ordinary radical neck dissection. The complete submental triangle cannot be seen.

The average skin area covering the extent of a radical neck dissection ranged from 175 to 220 sq. cm. in a group of patients actually studied and averages 205 sq. cm.

In the past some radiotherapists have attempted to treat areas of a size comparable to this with doses of radiation of the order of 1 to 2 threshold erythema doses, either as a prophylactic in the absence of clinically demonstrable metastatic nodes or as a preoperative effort to attenuate the disease.

The three small circular portals represent an example of the technique employed in the treatment of multiple foci of metastasis. The combined area of these three portals represents the approximate safe maximum area which can be irradiated to reasonably high levels prior to operation.

In 1950, Sharp[117] and his group and others[5,28,38,94,114] touch briefly on a similar method of treatment, using roentgen rays. Doses up to 4,000 r are used. They report no instance of impaired wound healing.

Because of the scant literature dealing critically with the subject of neck dissection performed after varying doses of roentgen radiation, there appears to be ample justification for this presentation.

In the management of oral cancer with associated lymph node metastasis, it must be appreciated that if the primary lesion is to be treated by irradiation methods, the cervical metastasis cannot be left to go untreated while the primary lesion is being controlled. Metastasis is the key problem in the management of oral malignancy.[18,20,21] Delay in its treatment should not be a part of any rational management. On the other hand, it should be appreciated that a radical neck dissection is rarely to be performed unless the primary lesion has been controlled or unless a combined operation is done in continuity. Therefore, while the primary lesion is being

irradiated, the metastasis, too, must be treated. The standard procedure appears to be to deliver irradiation in such a way as to treat the metastasis entirely by irradiation, either roentgen irradiation alone or roentgen irradiation followed by interstitial radium or radon.[2,4,32,38,71–82,102,103,105,106,111]

In 1944, in the belief that irradiation methods alone were too conservative an approach for the management of so grave a condition as operable neck node metastasis (based on the best available survival rates), the senior author began testing the feasibility of radical neck dissection after varying dosage levels of irradiation were given to selected patients presenting metastatic lymph nodes, in the hope of improving the poor results reported in the literature.[17,18,21]

The dose of radiation delivered to the metastatic disease is based on the response of the metastatic masses to treatment and the response of the primary lesion to treatment. The principle of treatment is not necessarily to sterilize the known metastatic disease (although this would of course be an acceptable result of such treatment). The principle and hope of treatment are to neutralize the metastatic disease temporarily while the controllability of the primary lesion is being demonstrated. In other words, a holding therapeutic action is fought in the neck while the major preliminary therapeutic action is carried out in the mouth. If the primary lesion can be controlled, decisive action can then be brought to bear in the cervical region. A radical neck dissection can then be done.

Technique. The primary lesion is controlled by precision peroral roentgen therapy and external portals when needed.[16,19,22] In many instances radon implants are used. External irradiation to the primary lesion is employed only if strictly needed. The total tumor dose to the primary lesion is 6,000 to 12,000 r—occasionally higher. The portals employed in the treatment of the cervical metastasis are used whenever feasible to the primary lesion as well. Excisional surgery occasionally is necessary after irradiation.

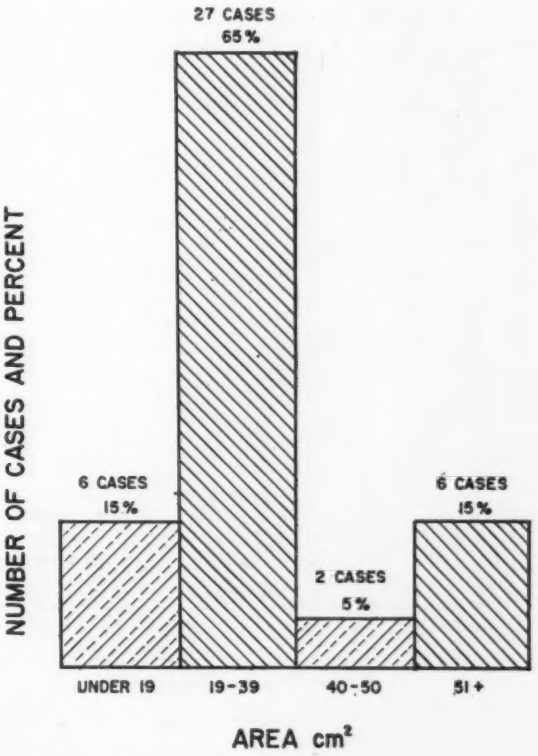

CHART I. Area of treatment portal (cm²).

Size of Cervical Portal. The portals used in treating the lymph node metastasis are rigidly controlled as to size. The portals seldom exceed by more than 1 cm. the diameter of the mass. Chart 1 gives a clear-cut view of the average portal sizes employed. The majority (65 per cent) of treatment portals measured 19 sq. cm. to 39 sq. cm. Only 15 per cent of cases had portals measuring under 19 sq. cm. Twenty per cent had portals over 40 sq. cm. in area. If more than one cervical metastatic lymph node is present, each node is treated separately. Such technique is better than one which attempts to treat through one larger portal all of the metastatic nodes. This is done to keep the area of treatment as small as possible (Fig. 1).

In 59 per cent of the treated cases, only one portal was employed to treat a single metastatic mass. Twenty-four per cent of

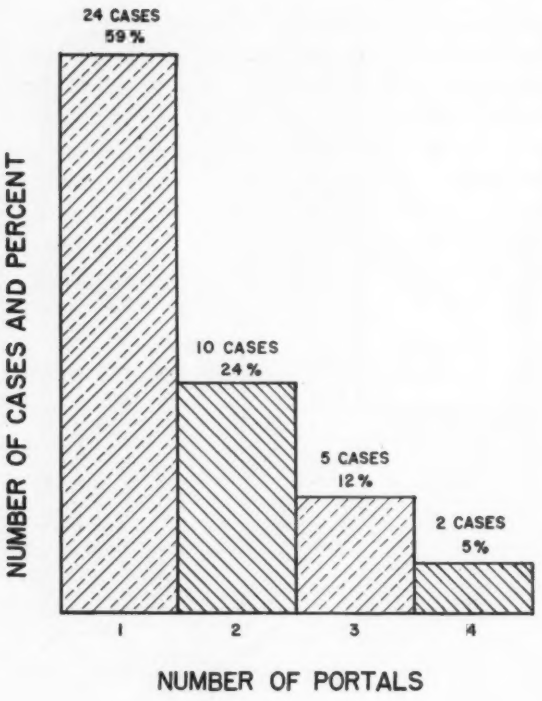

CHART II. Number of portals.

cases required two portals; in 12 per cent three portals were used and in 5 per cent four portals were used. These multiple portals are each treated daily (Chart II).

In 4 cases the total area of all cervical portals ranged between 64 sq. cm. and 72 sq. cm. Total portal areas of this size are not generally to be recommended. In one case where the portal areas exceeded 84 sq. cm. complete healing failed to take place during the period the patient remained under observation. In this patient infection played an important part. An emergency tracheotomy was necessary during the operation and bronchial secretions and mucus were spewed over the open dissection. Nevertheless, we do not favor irradiating areas over 70 sq. cm. with doses over 3,000 r (in air).

Administration. If the cervical portal or portals cannot be usefully employed in the ancillary treatment of the intraoral lesion, the dose in depth is diffused after passing through the metastatic mass. This can be accomplished by "wobbling" the treatment beam. That is to say, one day the beam is straight down, the second day the beam may have a 30 degree cephalic projection, the third day the treatment is given with a 30 degree caudal projection, the fourth day 30 degrees posterior projection, etc. Lower in the neck the treatment is never projected with anterior angulation. If the cervical portal can be utilized in treating the primary lesion, generally it is so used.

Dose. The average dose (measured in air) delivered to the cervical metastasis was 5,300 r. The highest dose was 11,000 r (Table IV). Thirty per cent of cases received a dose between 3,000 and 4,500 r (in air), while 46 per cent received a dose between 4,500 and 7,000 r (in air). Seventy-five per cent of cases received 3,000 to 7,000 r (in air) delivered in from fourteen to sixty-six days (Chart V). A moist to ulcerative epidermitis was always produced (Fig. 2).

The average tumor dose in the series was found to be 4,300 r, while the highest tumor dose was 10,533 r (Table IV). Chart IV shows the range in which most of the cases treated fell. Forty-one per cent of the treated cases received a tumor dose of between 3,000 and 4,500 r, and 34 per cent

FIG. 2. Example of moist ulcerative radiation epidermitis in three portals, as indicated by numbers. This patient received doses of 3,000 r, 4,200 r, and 4,200 r plus radon seeds prior to surgery. The approximate area of treatment was 45 sq. cm. This represents an average case.

received a tumor dose of between 4,500 and 7,000 r.

The cases which have received unusually high doses were originally selected for pure radiation management. These exceptional cases were finally operated on because of extending metastatic disease. Further radiation management with curative intent seemed a less practicable method in consideration of various factors involved.

Based on our experience, doses in excess of 7,000 r to an area larger than 30 sq. cm. seems undesirable. In routine cases, such doses are not needed to achieve the immediate objective of the irradiation. In addition, as has been already mentioned, where neck dissection is contemplated, we do not favor delivering radiation dosage in excess of 3,000 r (in air) if the areas total much over 70 sq. cm. Large areas are not made up of one circular portal or square portal, but rather of one, two or more smaller portals (Fig. 1).

Protraction of Dose. When first employing the technique herein described, treatment to the metastatic disease was considerably more protracted. Today the desired dose is delivered more rapidly—in three to five

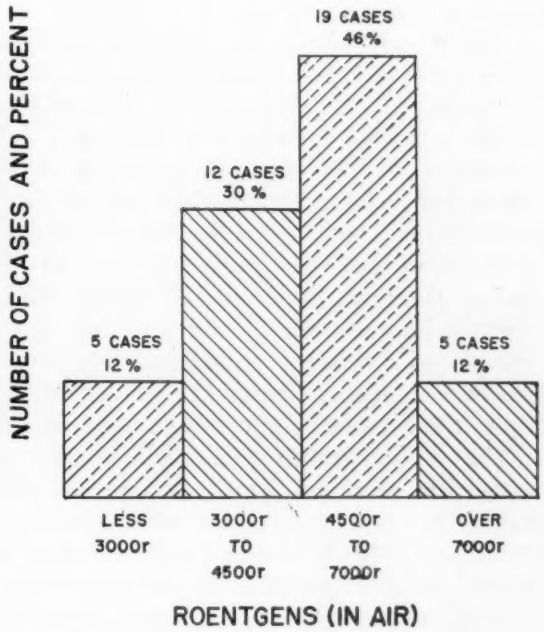

Chart III. Dose (in air) to cervical area.

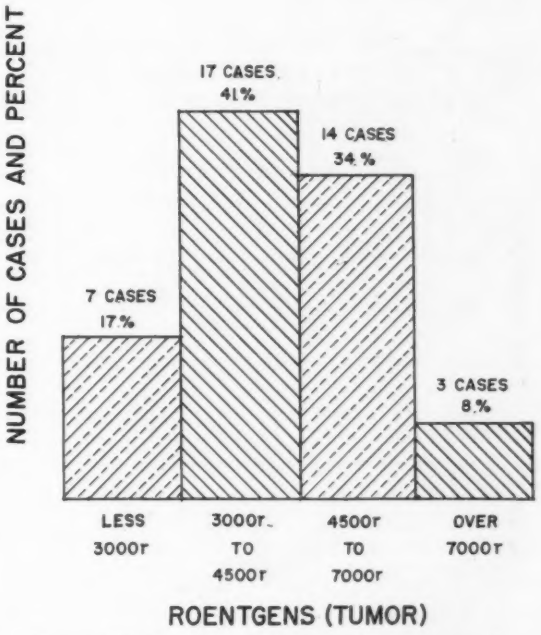

Chart IV. Dose (tumor) to cervical metastasis.

weeks. The dose protraction as measured against dose for each case is shown in Chart v. The dose varies somewhat, depending on the response of the metastasis and the difficulties involved in controlling the primary lesion.

It should be remembered that the objective is to control temporarily the cervical metastasis to permit the later performance of a neck dissection. Therefore, two problems exist: first, the metastatic disease must be contained; second, this must be accomplished with a dose delivered in such a way and to a dosage level which later *will not compromise the safe performance* of a neck dissection. In the series of cases studied, the average time to deliver an average dose of 5,300 r (in air) to an average area measuring approximately 30 sq. cm. was thirty-eight days (Table iv) (Chart v). In only 65 per cent of cases was the dose delivered in a period under five weeks. However, in 92 per cent of the cases the treatment time was approximately two months or less.

Delay Interval (Completion of Treatment to Operation). After completion of irradiation to the cervical metastasis, the sched-

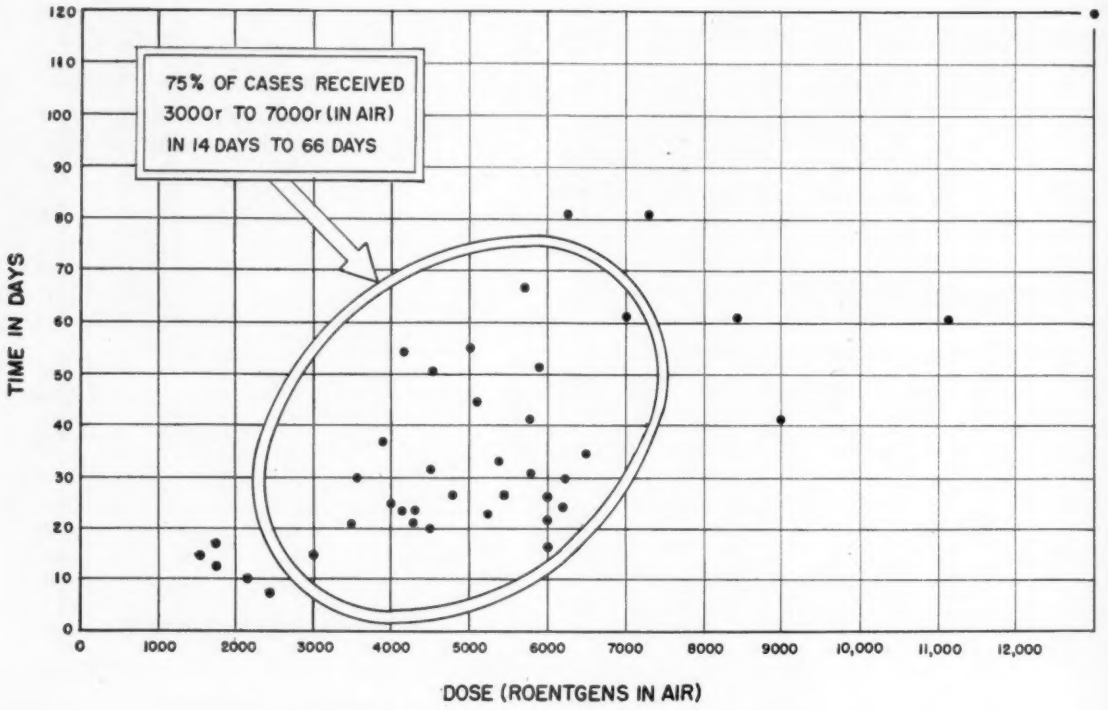

CHART V. Dose (in air) compared with total treatment time.

uling of the operation must await the healing of the moist epidermitis which always develops. It is axiomatic that we await the control of the primary lesion. It is necessary in some cases to delay the operation a short period in order to improve the general condition of the patient. The average interval elapsing from the time of completion of therapy of the cervical metastatic nodes to the time of operation was seventy-six days (Table IV). Three cases with unusually long intervals increase the average interval to this long period. The average interval between end of treatment until the operation would drop to less than fifty days if the few unusual cases with abnormally long intervals were excluded. These few exceptional cases were to have been treated purely by roentgen irradiation and radon implants. But because of spreading metastasis contiguous to the treatment portals months after the original treatment, neck dissections were done. Too long a period of delay definitely increases the technical difficulty of the operative procedure. Ideally, the operation should be performed as soon after healing of the epidermitis as is possible. Three to six weeks after completion of therapy is ideal; eight to ten weeks is acceptable. Some of our intervals ran considerably longer. Neck dissection may be held up, pending control of the primary lesion, efforts to improve the general condition of the patient, etc. Delay beyond eight to ten weeks will lead to increasing fibrosis.

Technical Difficulty of Operation. It is generally believed that delicate surgical procedures which follow intensive ionizing irradiation, such as roentgen, radium or radon therapy alone or in combination, greatly increase the difficulty of any contemplated operative procedure. One often hears a surgeon comment, for example, upon the fibrosis he encounters in performing a radical mastectomy following preoperative roentgen irradiation or on the difficulty of thyroidectomy after roentgen treatment. References in the literature are made to the tremendous difficulties involved in surgical procedures after irradiation.

TABLE I

TIME REQUIRED FOR HEALING

	Bilateral Suprahyoid				Radical Neck Dissection				Combined Operation			
	Without Roentgen Therapy		With Roentgen Therapy		Without Roentgen Therapy		With Roentgen Therapy		Without Roentgen Therapy		With Roentgen Therapy	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Under 24 days	3	100	4	50	14	58	11	39.0	2	34	0	0
24–36 days	0	0	0	0	5	21	4	14.0	3	49	1	50
36–60 days	0	0	4	50	5	21	7	23.5	1	17	0	0
Over 60 days	0	0	0	0	0	0	7	23.5	0	0	0	0
Never healed	0	0	0	0	0	0	0	0	0	0	1	50

Our experience along this line has been interesting. One of us (S. G. C.) performed practically all the operations in this series. The evaluation of the difficulty of surgery, therefore, should be easier than if the operations were performed by a group. Approximately 85 per cent of the cases operated on which received preoperative therapy presented little or no appreciable technical difficulty at operation. Of 42 cases receiving intensive irradiation to cervical metastasis prior to neck dissection, only 7 cases offered appreciable technical difficulty and only 1 case showed marked difficulty at operation. Of the 7 cases offering appreciable difficulty, 3 cases had received *radon* therapy in addition to roentgen therapy. Three additional cases had markedly prolonged delay intervals between radiation therapy and operation. In the seventh case the daily dose was 500 r (in air); in all other cases, the daily increment was 300 r (in air). The only case offering marked technical difficulty was one in which radon seeds had been implanted following roentgen therapy. The total dose was exceptionally high and a prolonged interval followed before operation.

It may be concluded that the cases which presented some difficulty during operation generally were those in which the interval between completion of treatment and performance of operation was the longest and/or in which radon seeds were employed in addition to roentgen therapy. The radon cases all had a long delay before performance of the operation inasmuch as they were not originally selected for surgery. It must be emphasized, however, that only 1 case offered truly marked technical difficulty. Quite naturally, it should be clearly understood that the evaluation of the difficulty involved in any given operative case cannot be based exclusively on purely objective considerations which are easily measurable.

On studying 33 cases of radical neck lymph node dissection performed on patients who had received no prior radiation treatment to the neck, all cases but one were performed with little or no technical problem (Table II).

Operating Time (*Comparison of Irradiated with Nonirradiated Cases*). Judging from the average time required to perform the operations, there is little to choose between the cases which had received preoperative roentgen therapy as compared with those which did not. The average time required to perform the actual operation in the two groups was practically the same: with roentgen therapy, two hours and fifty-nine minutes; without roentgen therapy, two hours and fifty-four minutes[24] (Table III).

An explanation exists for this apparent mild paradox. In the cases which had re-

TABLE II

NECK DISSECTION
TECHNICAL DIFFICULTY OF OPERATION

	With Roentgen Therapy (41 cases)	Without Roentgen Therapy (33 cases)
Little or no difficulty	33	32
Moderate difficulty	7	1
Marked difficulty	1	0

ceived roentgen therapy and in which difficulty was encountered during the course of the dissection, several things were done which tended to shorten the operative time. Actually, the chief purpose of the modifications in the operation was not to save time, but rather to perform a more adequate cancer operation.[6,7,8,13,14,15,27]

Most of the gross metastatic lymph nodes in operable cases are encountered in the upper neck. Irradiation is therefore delivered to this upper cervical area. If difficulty in dissection is encountered, it is therefore generally encountered in the region of the posterior belly of the digastric and the stylohyoid muscles. The surgeon is faced with the problem of deciding whether to attempt to dissect the muscles away from the mass of tissue to be sacrificed or to sacrifice the muscles.[32,36] The senior author removes the above muscles en masse with the sacrificed mass of tissue. Frequently, the external carotid artery is resected.[33] The spinal accessory nerve is preserved only in special cases where it is felt that the tunneling through the sternocleidomastoid muscle does not compromise fundamental oncologic operative precepts.[51,55,60,61,118,121] In cases of metastasis developing after control of the primary lesion where roentgen irradiation has not been given, more thought is given to preserving the digastric or at least the stylohyoid muscles and to the preservation of the spinal accessory nerve. Not infrequently, however, if the situation and extent of the metastatic disease seem to indicate, the procedure as described above is followed, even in the nonirradiated case.

TABLE III

NECK DISSECTION
AVERAGE TIME OF OPERATION*

With preoperative roentgen therapy	2 hr. 59 min.
Without preoperative roentgen therapy	2 hr. 54 min.

* Anesthesia—cervical nerve block.

It may be mentioned here that when feasible some of the irradiated skin is removed—never, however, to an extent that a relaxed closure is not possible. Once in a great while it may be necessary to remove so much skin in doing a neck dissection that a flap must be employed to achieve closure. This has been done with complete success in 2 instances of combined operations using posterior scalp flaps.[127]

Few patients complain after loss of the spinal accessory nerve. An occasional patient, probably 1 in 20, will complain of shoulder ache, not often severe. Removal of the posterior belly of the digastric and the stylohyoid muscles causes some slight difficulty on occasion. A shift of the neck structures is noted.

Time Required for Healing after Operation. The literature refers not only to the difficulties involved in the performance of radical operative procedures in the neck after intensive irradiation, but points to the disastrous results which may follow such operations. Our experience over the past six years with intensive irradiation followed by radical surgery does not add weight to the above opinions. It has already been pointed out by us that surgical procedures not only can be done after controlled and planned preoperative roentgen irradiation, but that they can be performed with little appreciable increased difficulty. The time required for complete healing of these radical operations performed on necks which have been subjected to intensive doses of radiation has been studied by us with the following results:

The average complete healing time required for the neck dissection cases which had received *no previous* irradiation was

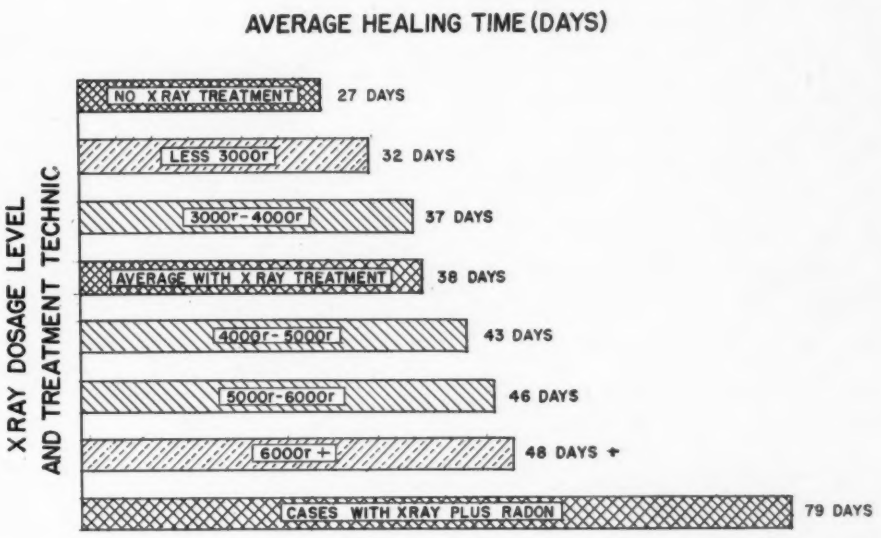

Chart VI. Cervical node dissection healing time compared with dosage and various treatment techniques.

twenty-seven days (control series, 33 cases).

The average complete healing time for the neck dissection cases which had been given varying doses of *preoperative* roentgen irradiation was thirty-eight days, an average of only eleven days longer, despite the inclusion in this study of radon treated cases.

The average complete healing time for the neck dissection cases which had received varying doses of roentgen irradiation followed by radon seed implantation was seventy-nine days (Chart vi).

About 58 per cent of nonirradiated cases healed in twenty-four days or less, as compared with 39 per cent for the irradiated cases (Table 1). Seventy-nine per cent of the nonirradiated cases healed in thirty-six days or less, while 53 per cent of the irradiated cases healed in thirty-six days or less. About 23 per cent of the irradiated cases required over sixty days to heal, whereas no cases in the nonirradiated group required over sixty days (Table 1).

Based on our experience, a dose up to 5,000 r (in air) is fairly well tolerated. An average complete healing time of forty-three days, which is sixteen days longer than the average time required for complete healing in the control series, certainly cannot be used as an argument against the performance of neck dissection.

Examining more closely into the healing time of the roentgen irradiated group, it is learned that cases receiving less than 3,000 r (in air) healed about as well as the nonirradiated group—thirty-two days as compared with twenty-seven days (Chart vi). As the dose in air increases, the healing time increases accordingly. With a dose between 4,000 and 5,000 r (in air) an average interval of forty-three days is required for healing. When the dose exceeds 6,000 r (in air), the healing time increases to more than forty-eight days. At this point, using conventional roentgen-ray beams of the order of 200 kv. (peak), a dose exceeding 6,000 r (in air) to portals of the size described is not recommended (Chart vi). Possibly with roentgen-ray beams generated at levels of 1.75 megavolts or more, considerably higher doses to larger areas may be given with equal or comparable safety. Our short experience of two years with such quality of radiation permits of no conclusions.

Number of Positive Lymph Nodes and Irradiation Effect. All of the gross and microscopic specimens were studied by our pathologist, Andrew J. Donnelly.[31] About

TABLE IV

CERVICAL LYMPH NODE METASTASIS
TECHNICAL FACTORS OF IRRADIATION

Area		Air Dose		Tumor Dose	
Largest	83.5 sq. cm.	Highest	11,100 r	Highest	10,533 r
Average	29.1 sq. cm.	Average	5,300 r	Average	4,300 r

Time to Deliver Radiation		Interval Roentgen Therapy to Operation	
Longest time	158 days	Longest interval	220 days*
Average time	38 days	Average interval	76 days
		Shortest interval	21 days

* See text.

91 per cent of cases showed microscopic evidence of metastasis. The percentage of cases which showed only one positive lymph node in the specimen (evidence of metastasis) was about the same for the two groups: for the irradiated group, 54 per cent; for the nonirradiated group, 53 per cent. Two positive lymph nodes were found in 32 per cent of the irradiated cases and 23 per cent in the nonirradiated group. Three to five positive nodes were found in 14 per cent of cases which had received preoperative irradiation. In the control series, 24 per cent of cases had from three to four positive nodes. It can be seen that the two groups are closely comparable in that the percentage incidence of metastatic involvement to single and multiple nodes is seen to be quite similar in the two groups under comparison. In the control series, however, the metastatic nodes developed after control of the primary lesion (Table v).

TABLE V

NUMBER OF POSITIVE LYMPH NODES

Number of Nodes	With Preoperative Roentgen Therapy (41 cases)	Without Preoperative Roentgen Therapy (27 cases)
	per cent	per cent
1	54	53
2	32	23
3	10	6
4	2	18
5	2	0

Various cytological and histopathological changes are produced in the lymph nodes which have undergone intensive ionizing irradiation, the most interesting of which is keratogenesis. Apparently one function of ionizing radiation is to enhance spontaneously occurring keratogenesis, and sometimes the effect is so complete that the carcinoma is rendered sterile as a neoplastic growth. The achievement of complete or even increased morphologic differentiation (keratin is the end product of complete morphologic differentiation) in squamous cell carcinoma serves to combat the neoplasm since it reverses at least one characteristic deviation of such malignant disease, which is the failure to differentiate morphologically in the balanced rate that is maintained in the normal counterparts.*

END RESULTS

1. *Material.* The 42 patients who make up the irradiated group are selected because of the fact that they received irradiation prior to neck dissection. The cases were operated on from 1944 to 1950. During that time, approximately 441 cases of oral malignancy were treated, with about 143 cases presenting metastasis on admission.

The criteria of operability followed in this series conformed quite closely to those of Duffy. In other words and generally

* These remarks have been abstracted from an unpublished paper by Dr. Andrew J. Donnelly, Pathologist at the American Oncologic Hospital.[31]

speaking, the cases herein selected for irradiation to the metastatic nodes followed by neck dissection, in general presented the same extent of metastatic disease as cases which would have been selected for operation had the metastasis first presented after control of the primary. It should be mentioned that patients who received intensive irradiation to relatively large face portals nearly always were treated as pure irradiation problems. The control series, made up of neck dissection cases which did not receive preoperative irradiation, comprises 33 cases. Metastasis appeared after treatment to the primary lesion. These cases were operated on in the same period as the irradiated group (1944 to 1950).

2. *Site of Local Lesion.* It is well known that the end results in the management of oral carcinoma are variable, depending, among other things, upon the site of the primary lesion. Carcinoma of the lip offers by far the best outlook. Carcinoma of the tongue, particularly the more posteriorly placed lesions, offers a far poorer prospect for cure. The percentage incidence of the lesions involving the various sites is surprisingly comparable. For example, in the nonirradiated group, 18 per cent of cases were cancer of the tongue and 29 per cent were of the floor of the mouth; in the irradiated group, the figures were 19 per cent and 24 per cent. Inasmuch as the number of cases in each category is too small to be of significance taken separately, the lumping of cases seems justifiable in view of the unusually close comparability of the two series, based on the site of the lesion (Table VI).

TABLE VI

NECK DISSECTION IN ORAL CANCER
SITE OF LOCAL LESION

	With Preoperative Roentgen Therapy (41 cases)	Without Preoperative Roentgen Therapy (30 cases)
	per cent	per cent
Cancer of lower lip	13	19
Cancer of tongue	18	19
Cancer of buccal surface	13	19
Cancer of floor of mouth	29	24
Cancer of gingiva	18	0
Cancer of palate	0	19
Cancer of tonsil	9	0

TABLE VII

NECK DISSECTION IN ORAL CANCER
CAUSE OF DEATH

	With Preoperative Roentgen Therapy No.		Without Preoperative Roentgen Therapy No.	
1. From original cancer	14		8	
Recurrence at primary site	7	14	4	8
Neck recurrence	2		1	
Crossed metastasis	3		0	
Distant metastasis	2		3	
2. Postoperative	2		0	
3. A second primary cancer				
Primary cancer of the lung	1		0	
Hypernephroma	0		1	
4. Nonmalignant deaths	3		1	

3. *Results.* The two series which have been shown to be quite comparable in several respects is comparable in still another respect. The control series (without preoperative irradiation) contains no cases operated on prior to the date of operation of the first case which had received preoperative irradiation. In other words, the two series parallel each other from the time standpoint.

The authors recognize that the two series are too small and have not been followed long enough to draw final conclusions. It seems fair nonetheless to present our results as they appear to date.

A comparison of end results of various methods of managing cervical metastasis* from oral malignancy is now under way by the authors.

The purpose in presenting the treatment results of the two series (series with irradiation and series without irradiation) is to contrast the results in a poorer

* Present on admission with associated uncontrolled primary lesion.

TABLE VIII

NECK DISSECTION
END RESULT STUDY

	With Preoperative Roentgen Therapy		Without Preoperative Roentgen Therapy	
	No.	Per Cent	No.	Per Cent
Living without disease*	17	41.5	6	35
Died of disease (or due to)	15	36.5	8	47
Died without disease	5	12	2	12
Lost to follow-up without disease	4	10	1	6

* Cancer.

prognosis group with the end results in a group where the prognosis should be more favorable.*

Of the 41 cases which received preoperative roentgen therapy, 41.5 per cent were alive for varying periods of time without evidence of disease. Four cases (10 per cent) were lost to follow-up without evidence of disease, and 5 cases died without evidence of cancer after varying intervals of over one year. Fifteen of the 41 cases died as a result of cancer.

Of the 32 determinate cases, 17 cases are alive for varying periods up to six years without evidence of malignant disease (53 per cent). Thirty-two per cent are alive and well for periods of three to five or more years (Tables VIII and IX).

Only 21 per cent of cases in the nonirradiated group are alive and well for periods of three to five or more years compared with 32 per cent in the irradiated group. Of the living determinate cases, 43 per cent compared with 55 per cent are alive and well from one to six years.

Cause of Death.

Irradiated Group: Of the cases receiving radiation therapy to the neck prior to neck dissection, 15 cases died directly or indirectly as a result of the primary malignant disease. Death resulted from recurrence of the primary lesion in 7 cases. Death was attributable to recurrence in the neck after neck dissection in 2 instances. Crossed cervical metastasis could be considered the cause of death in 3 cases. Two patients died from visceral metastasis.

One patient died from hemorrhage many months after operation. The patient, a severe hypertensive, with an amazingly tortuous common carotid artery, developed a small trophic ulcer through which the common carotid artery ruptured quite unexpectedly.

One patient died of a totally new cancer —primary cancer of the lung (Table VII).

Of the 2 postoperative deaths, both cases

TABLE IX

NUMBER YEARS ALIVE AND WELL
(No. Cases and Per Cent Determinate Cases)

	With Preoperative Roentgen Therapy			Without Preoperative Roentgen Therapy		
	No.	Per Cent		No.	Per Cent	
Over 5 years	3	9.5	32	2	14	21
3–5 years	7	22.5		1	7	
1–3 years	6	20		2	14	
Less than 1 year	1	3		2	14	

Per Cent Determinate Cases Living and Well
With preoperative roentgen therapy 55%
Without preoperative roentgen therapy 43%

* The group in which no irradiation was delivered should have much the better prognosis, inasmuch as the primary lesion has already been treated and brought under control and has remained under control.

died of cardiac failure. The fact that these 2 patients received irradiation played no part in the death of either patient. One of these patients was past eighty years of age.

Nonirradiated Group: Ten deaths attributable to cancer occurred in the group of patients which did not receive neck lymph node irradiation prior to neck dissection.

There were no postoperative deaths.

Three cases died as a result of distant metastasis.

One patient died of a totally new cancer —a hypernephroma (Table VII).

DISCUSSION

Many surgeons and radiologists who treat oral malignancy believe that radical surgical procedures on the neck, such as radical neck dissections, are technically impossible or unacceptably hazardous, if attempted after intensive radiation therapy. In consequence of this belief, a patient with oral cancer complicated by cervical metastasis on admission is considered by most physicians as a pure irradiation problem, if the local lesion is to be treated by irradiation methods. This pure irradiation technique has been adhered to in the past by those who believe strongly that radical neck dissection is the treatment method of choice if metastasis develops after control of the primary lesion. These men then must agree that neck dissection is unfeasible after intensive radiation therapy to the neck.

The senior author believed that irradiation methods alone were too conservative an approach for the management of so potentially grave a condition as cervical metastasis. An effort has been made to explore the possibilities of combining precision irradiation and radical surgery in the treatment of metastasis.

The principle of management is to carry out a holding action in the neck while the primary cancer is being destroyed. If and when the primary lesion is controlled, decisive action can be brought to bear on the cervical metastasis. A radical neck dissection can then be done.

Few significant contributions to the medical literature can be found dealing critically with this subject. Perhaps the most detailed report comes from Engelstad of Norway. In 1938 and 1945, Engelstad, who employed preoperative teleradium therapy, was enthusiastic in support of his treatment methods.

In view of the scant literature dealing with this subject and the complete absence of critical study to support the strong negative conclusions invariably drawn, the authors, in view of their experience with a technique of intensive irradiation followed by neck dissection, feel that a critical review is worth while.

It may be stated that if portals are used which are not too large—up to 60 sq. cm. —or doses are used which range from 4,000 r (in air) to a maximum of 6,000 r (in air), a radical neck dissection is a perfectly feasible procedure. The safe dose drops to 3,000 r (in air) when the area reaches 70 sq. cm. Larger areas are not advised.

The irradiation should be fractionated at a rate of 300 r per day. Conventional deep roentgen therapy (200 kv., peak) was used in our cases.

The interval after completion of irradiation to the neck to the time of operation should not be too long delayed. The optimum time is within three to six weeks of the completion of radiation therapy or of the healing of the moist epidermitis (Fig. 2). Radon seeds are not ordinarily recommended as a preoperative method of management unless the operation falls within a period of two weeks of the implantation. Increased operative difficulty and markedly prolonged healing time follow its use if surgery is delayed.

The average complete healing time of the neck dissections in cases receiving intensive roentgen irradiation is not significantly longer on the average than a control series which did not receive irradiation—thirty-eight days compared with twenty-seven days.

The operating time (time consumed at operation) was practically the same (179

minutes) for the cases receiving irradiation as compared with 177 minutes for the control cases.

It may be stated that local anesthesia was used exclusively in these cases.

Of the deaths attributable to the operation, 2 deaths occurred in the group receiving irradiation (41 cases), while no deaths occurred in the control series (33 cases). It must be emphasized, however, that both deaths could in no way be attributable to the irradiation. The combined operative mortality was 2.8 per cent.

The series studied is too small to permit of drawing conclusions. However, comparing the determinate survival rates of the cases receiving irradiation prior to neck dissection with a control series in which metastasis developed after control of the primary oral cancer and in which irradiation did not precede the neck dissection, the results favor the irradiated series. This is true despite the fact that the irradiated group is made up of the most unfavorable cases. The results are closely comparable to those of Engelstad of Norway, the only other worker who has apparently enthusiastically championed a similar method of treatment.

CONCLUSION

It seems reasonable to conclude that if the method of treatment of metastasis described herein is closely followed, the procedure is entirely safe and may improve considerably the end results in the most favorable or operable cases of oral malignancy which present metastasis when first seen. The authors strongly believe that irradiation methods alone are too conservative an approach for the management of operable metastasis. Those cases of metastasis where the prospects for cure seem brightest are those in which the technique herein described may prove most applicable. There is no reason to believe that the management of cervical lymph node metastasis should not be carried out as radically as is consistent with fundamental oncologic concepts as practiced in other areas of the body.*

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* For discussion see page 802.

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RADIUM IN THE TREATMENT OF CANCER OF THE TONGUE*

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THE place of interstitial radium therapy in the treatment of cancer of the tongue is apparently being challenged again both by surgeons and roentgen-ray enthusiasts and perhaps it behooves those of us still interested in this modality to review this treatment agent and the techniques of using it rather critically.

The surgical argument is based upon the 28 per cent five year survival rate reported by the great English surgeon, Butlin,[2] over forty years ago, a record which has not been equalled by later surgeons. Furthermore, the surgical figure is based upon the survivals of those patients who were operated upon and not upon the total number of patients entering the clinic with the given diagnosis. The radiotherapist attempts at least palliation on practically every patient and calculates his survival rate upon the total number. When the cases are broken down into groups and only those used who would be possible candidates for radical surgery, the radiation results are seen to be far better than 28 per cent. A second difficulty encountered in the surgical approach is the deformity and resultant speech defect inherent in the removal of any appreciable amount of the tongue substance. Surgery will actually need to show a really statistically significant survival improvement over irradiation before it can justify this functional loss.

Everyone admits that conventional external irradiation is not effective, but certain groups have been using and advocating external irradiation with radium bombs or roentgen therapy units in the 700 to 2,000 kv. range. The only large series reported to date is that of Berven.[1] His results are impressive but he admits that electrocoagulation is used on persistent remnants of tumor in almost every case. He thus achieves a small improvement in survival rate at the expense of surgical mutilation added to a severe irradiation ordeal.

Unfortunately, it is impossible to evaluate the various interstitial radium techniques on a direct comparison basis because no uniform classification of stages and types of disease has been adopted and there has not been sufficiently detailed reporting of the complications, ill effects and failures met with in various clinics. Nevertheless, a study of the literature accents personal experiences so that certain technical aspects assume significance in relation to end results, and I believe it important that we emphasize these points, particularly in the practical and didactic teaching of our residents and fellows.

Preliminary external and peroral roentgen irradiation has definitely improved results and simplified technique. As Sharp and his co-workers[3,4] have rightly emphasized, cancer of the tongue is an aggressive disease demanding prompt action. One does not wish to undertake treatment as radical as interstitial needle implantation without biopsy confirmation of the diagnosis. Roentgen irradiation is a much less drastic procedure which can be started at once and carried on until the diagnosis is established. During this period, the lesions become cleaner and the subsidence of edema often reveals the limits of the lesion with considerably greater clarity. During this period the lesion can be studied and the radium therapy planned with care. Finally, the devitalizing effect of this irradiation probably reduces the ability of cells dislodged during the implantation to survive

* Presented in a Symposium on the Head and Neck at the Thirty-third Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–9, 1951.

and grow in remote locations. The direct peroral route is to be preferred whenever the lesion can be brought well within the field of an adequate cone. Otherwise external roentgen irradiation must be used. The direct intraoral cone has the great advantage that it avoids a general mucositis and damage to the teeth.

The optimum linear intensity has never been clearly demonstrated experimentally or statistically, and one finds strengths all the way from 0.5 mg. per centimeter to 5 mg./cm. being used. There can be no doubt that with the present scarcity of hospital beds and the cost of even ward care, the 5 mg./cm. needle has a great economic advantage. The patients are understandably less reluctant to have a mouthful of needles and threads for twenty hours than for 200 hours. The shorter duration of pressure ischemia and open portals for infection has been proved to result in less immediate cellulitis and infection. This difference is sufficiently great, for example, so that one can use such needles in the nose and ear with no fear of chondronecrosis. However, there is another side to the story. The higher intensity of radiation is definitely more damaging to normal tissue. Thus, the therapeutic ratio is reduced and dosage calculations must be made with great care if one is to avoid radionecrosis. It has generally been assumed that the cancerocidal dose is about 7,000 gamma roentgens, the assumption being based on the old empirical work with radon where 1 millicurie destroyed was a common dose. Experience with the 5 mg./cm. needles in our clinic in the past five years has shown that such dosage carries with it the probability of radionecrosis of some degree in over half of the cases. Our series is too small to allow a significant analysis of five year end results but already it is apparent that they do not justify the danger of necrosis which goes along with the use of 5 mg./cm. needles. In experienced hands, the technique can be used to advantage when other conditions make it difficult to leave needles in place for several days, but it must be undertaken with caution. I am convinced that intensitities of 1 to 2 mg./cm. are safer as well as more efficacious. If the higher intensity is used, dosage should be kept to 6,000 gamma roentgens or less. This dosage also must be correlated with the roentgen-ray dosage and care taken that the total does not exceed the equivalent of 10 erythema tissue doses. Another way of approaching it would be to say that if we consider 4,000 r a tolerance dose for our field size and radiation quality and we give 2,000 r or 50 per cent and 6,000 gamma roentgens as tolerance for the 5 mg./cm. needles, then we should give only another 3,000 gamma roentgens to the patient.

Probably the greatest cause of failure lies in the technique of inserting the radium needles. This is one of the most difficult tasks in radium therapy and unfortunately only a few people treat enough cases to become really proficient. The first common error occurs before the needles are inserted. The operator underestimates the depth of the lesion and employs needles which are too short. The active length of the needles must be at least as long as that diameter of the tumor in which the needles are being inserted.

The second common error arises from a lack of appreciation of the structure and motion of the tongue. The tongue is a highly plastic, intricate mass of muscle bundles which move in all directions and which have no rigid point of fixation. The hyoid and mandible both move and in moving deform the tongue. The division of the tongue into an anterior mobile and a posterior fixed portion exists only in the imaginations of medical writers. The entire tongue moves. The superior muscle bundles move more than the deep ones. The center moves more than the sides. If there is any system to the tongue it is probably best described by likening it to a set of paraboloid or ellipsoid springs with all ends fastened to the hyoid. As one pulls on the anterior portion of the loops, the coils roll up and forward about this anchorage with the mid-portions assuming a flatter contour

almost tangential to the vertical radius of the coils. At the same time, the lateral coils swing inward and flatten somewhat less than the center ones. These characteristics would not be too important if the tongue could be left in a relaxed neutral position during the insertion of the needles. Unfortunately, it is usually necessary to pull the tongue forward when inserting needles behind the middle. If these posterior needles are to stand vertically when the tongue is relaxed, they must be inserted at a sharp angle, point backward, when the tongue is pulled out, and this angulation must be greater for medial needles than for lateral ones. Needles in a rigid tumor will move upon relaxation of the tongue less than those in the surrounding muscle. Even the most experienced therapist cannot gauge the extent of all of these movements accurately. It is essential that true lateral and anteroposterior roentgenograms be taken and examined immediately after each implantation. The offending needles must then be removed, reinserted and checked at once before the anesthetic has worn off.

A third cause of nonhomogeneous radiation lies in the failure of the operator to provide good anesthesia, good lighting, and relaxation for himself and the patient. The best way to achieve these ends is to enlist the services of a dental colleague. The dental chair and light are ideal for work in the mouth. A dentist who is doing mandibular blocks daily will have far greater success with the simpler lingual block than the therapist who does only a few each year. Of course, local infiltration of the deep portion of the tongue must supplement the lingual block since the pain fibers accompanying vessels are not affected by the lingual block and one always gets pain deep in the tongue. In the posterior tongue only surface cocainization and local infiltration is indicated since this portion of the tongue is not supplied by the lingual nerve.

The division of the treatment into two portions with the needles being inserted vertically at one session and horizontally at the other is helpful in eliminating areas of low intensity, but it is an added ordeal to the patient and is frequently not mechanically feasible. In most cases, there is an optimal direction of implantation which, if carefully studied and fully exploited, will allow complete coverage of the lesion.

As stated above, our series is too small and too recent to allow statistical analysis. Over half of the implants have been done by radiology residents passing through my service. Some things such as the use of 5 mg./cm. needles were done on a deliberately experimental basis and have already been proved to be wrong. Eight out of 15 patients treated from one and a half to five years ago are living and apparently free of cancer. Only time can tell whether the results will be maintained or whether they can be improved.*

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* For discussion see page 802.

A STUDY OF CERVICAL LYMPH NODE METASTASIS IN SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY

WITH NOTES ON CLEARED AND FRESHLY DISSECTED SPECIMENS*

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PATHOLOGIC material obtained from neck dissections in squamous cell carcinoma of the oral cavity has been under study with the purpose of discovering more information about the early lymph node spread of this type of carcinoma. The practical application of this knowledge to early prophylactic cervical operations is considered, as well as the distribution and number of lymph nodes in relation to the extent of operations designed for removal. The number of patients is too small to permit of statistical review.

Materials and Methods. There were 33 patients in the series with various types of neck dissections. The sites of primary carcinoma were: lip, 7; tongue, 11; buccal mucosa, 7; floor of mouth, 5; tonsil, 1; upper gingiva, 1; and lower gingiva, 1. Six specimens were prepared and cleared after fixation as done by Gilchrist and David[1] and the remainder were either dissected out in the fresh state or removed from thin slices of Bouin's fixed tissue. All lymph nodes or suspected nodes were oriented for identification of position on the specimens and then submitted for routine histopathologic preparation. Finally, the histopathologic findings were compared with pertinent clinical data.

Anatomical Distribution and Number of Lymph Nodes. The lymph nodes were classified in two groups, one consisting of those above the hyoid bone, and the other of those below. Although it is recognized that more exact localization is desirable the lymph nodes were not always accurately oriented. Some operations were limited to the suprahyoid area. The well described wide distribution (Rouvière[3]) of cervical lymph nodes was confirmed. Lymph nodes were plentiful in the parotid, submaxillary, deep cervical and supraclavicular regions, and less numerous in the submental and trapezius areas. The great variations in the number of lymph nodes in the different patients were notable. In the suprahyoid site the number ranged from zero (2 patients with locally spreading infected tumor and with heavy irradiation) to 26, while below the hyoid the range was from 3 to 132. The average number of lymph nodes in the suprahyoid area for 39 specimens was 8 nodes per specimen, and in the infrahyoid area in 26 specimens the average was 36 nodes per specimen. The single highest total for a complete unilateral radical neck dissection was 146. Fewer lymph nodes were found in the 6 cleared specimens than in those dissected in the ordinary manner. The averages in

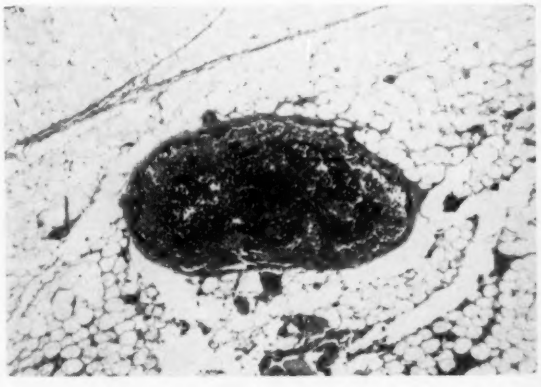

FIG. 1. Patient W. W. Normal lymph node, about 1.5 mm. in diameter, removed from fresh neck dissection specimen. (74× S.P. No. 78024 C)

* Presented in a Symposium on the Head and Neck at the Thirty-third Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–9, 1951.

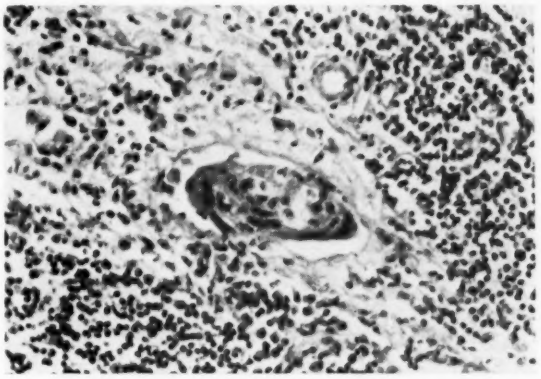

Fig. 2. Patient A. F. Squamous cell carcinoma of floor of mouth. Early metastatic focus in peripheral cervical lymph node sinusoid. (440× S.P. No. 65680 A)

the suprahyoid area were 7 (cleared) versus 8 (dissected), and in the infrahyoid area, 11 (cleared) versus 42 (dissected). The clearing method was not as accurate in locating lymph nodes or as fruitful in uncovering them as had been expected and this procedure was discontinued. The heavy cervical fascia and the bulky sternomastoid muscle prevented adequate clearing.

Pathologic Findings. Lip: Of 5 cases in the determinate group 4 showed cancer cells in or beyond the capsules of the involved lymph nodes and 1 with cells confined to the lymph node itself. Two of the patients are dead, 1 from each group. Both of these deceased patients had been known to have large submaxillary lymph nodes for over a year before operation. The remaining 3 patients, now alive and free of tumor for an average period of twenty-two months, had metastases which were known to have become clinically evident within two months before neck dissection. All patients obtained local control of the lip carcinomas. There were no positive lymph nodes below the hyoid bone. The average number of cancerous lymph nodes per patient was 4.4, with a range of 1 to 6.

Tongue: There were 5 patients in the determinate group, all of whom had spread of cancer to the capsule (1 patient) or beyond (4 patients). These 5 patients all died within eleven months of radical neck dissection. All except 1 had local control of the tongue cancer. In each case cancerous lymph nodes were found in the deep cervical chain, separated from the anterior scalene muscle and carotid artery by a thin film of connective tissue. All patients developed recurrence along the scalene muscle and carotid artery regions. The known duration of enlarged neck lymph nodes in the 5 patients varied from two to six months and averaged 4.8 months. The average number of cancerous nodes was 4.4, with a range of 1 to 14 per patient.

Buccal mucosa: Of 5 patients in the determinate group, 4 showed cancer within (1) or beyond (3) the node capsules. Two patients died—1 of these had a large deep cervical node for fourteen months prior to jaw-neck resection; the other had a malignant primary tumor not controlled by irradiation. The 3 patients still alive had lived thirty, thirty-one and five months after operation, completely free of tumor. The average number of cancerous lymph nodes was 3, with a range of 1 to 4. Local control was obtained in 4 patients.

There were not enough patients in the other groups for profitable analysis of their records.

Prophylactic Neck Dissection. Six patients underwent prophylactic neck dissection. In 3 with cancer of the tongue no positive lymph nodes were found. One of these patients died on the operating table (a jaw-tongue-neck resection was done simultaneously); the other 2 are alive and free of

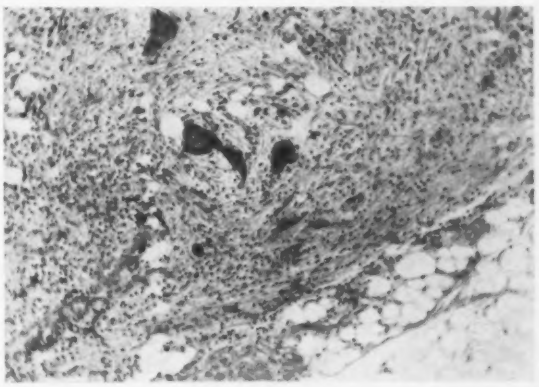

Fig. 3. Patient M.B. Squamous cell carcinoma of buccal mucosa. Prophylactic neck dissection. Submaxillary lymph node, 1.5 cm. in diameter, nonpalpable preoperatively, showing cancer cells in the capsule. (150× S.P. No. 85945 B)

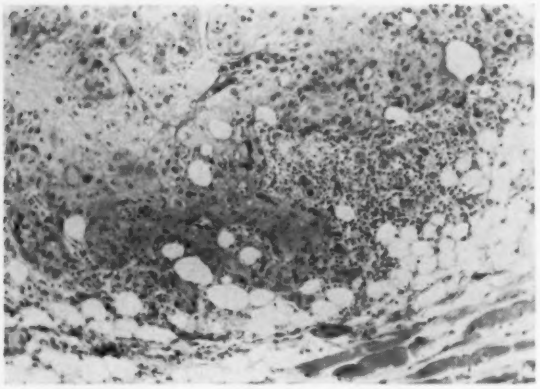

FIG. 4. Patient H.S. Squamous cell carcinoma of buccal mucosa with submaxillary lymph node metastasis. Cancer cells have extended through the lymph node capsule and lie adjacent to the platysma muscle. The need of removing the platysma is readily apparent. The patient is free of recurrence two years later. (150× S.P. No. 66558 C)

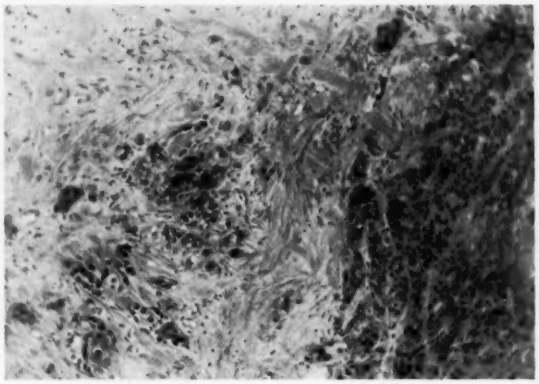

FIG. 5. Patient S.G. Squamous cell carcinoma of tongue metastatic to cervical lymph nodes. This node rapidly enlarged and became palpable nine months after healing of the oral wound following hemiglossectomy. The lymph node was greatly enlarged (3.0 cm. in diameter) due to tumor and fibrous tissue formation without evidence of infection. (150× S.P. No. 74940)

tumor fifteen and sixteen months later. Of 2 patients with cancer of the buccal mucosa, 1 showed a single positive lymph node with cells already invading the capsule. Both patients are well and free of tumor four and eleven months later. One patient with cancer of the floor of the mouth had a single positive submental lymph node. When he died thirty-three months later of peritonitis, autopsy showed a single cancerous node situated over the thyroid gland; 1 local recurrence had been successfully treated three months previously.

DISCUSSION

The recording of the number of lymph nodes present in the suprahyoid and infrahyoid regions of the neck has disclosed a wide range of variability. Some complete unilateral neck dissection specimens have yielded as few as 7 lymph nodes after thorough search, and others up to 146. Estimates of the total number of lymph nodes on one side of the neck in the areas ordinarily removed at radical neck dissection have been found by Rouvière[3] to vary from 23 to 48. This work was performed on cadavers by means of injection methods. There are few other reports of lymph node counts in the cervical region. The value of this pathologic study has been amply demonstrated. Clinically, it gives a greater impetus to the surgeon to be radical in planning neck dissections for oral cancer metastases and it serves as a record for the pathologist to equal or exceed in dissecting lymph nodes in each specimen, as well as adding more information in the management of each patient.

We were impressed with the paucity of lymph nodes involved by cancer, even in late cases, as noted by Taylor and Nathanson.[4] In most of the specimens only 1 to 6 cancerous lymph nodes could be found, and the multiple ones often were continuous and matted. In 1 patient with a rapidly progressing tongue cancer 14 positive lymph nodes could be found and several more were palpated on the contralateral side of the neck but not excised for histopathologic examination.

Since spread of metastatic carcinoma beyond the confines of a lymph node is often considered to be associated with a poor prognosis, our cases were analyzed with that in view. We have found that spread into or beyond the capsule of the lymph node did not always mean an early fatality. The determining factors of even greater importance may be the duration of the lymph node metastasis, failure to control the primary oral lesion, and the location of the lymph node in question.

In the patients in this series with cancer of the lip and buccal mucosa, 9 out of 10 patients exhibited spread within or beyond the capsule. Four of these patients died in from four to fifteen months. All had metastases which were external to the submaxillary salivary gland and which were resected with ample surrounding tissue. On the other hand, 5 patients with lingual cancer who had extension of cancer into lymph node capsules or beyond died within eleven months of operation. The deep cervical lymph nodes were the ones involved by cancer, and those nodes were contained only by thin filmy tissue adjacent to the carotid sheath and anterior scalene muscle, structures not ordinarily removed. The combination of deep cervical lymph node metastasis and penetration of the lymph node capsule in this small group of patients with cancer of the tongue has been found to lead to early death.

The propriety of performing prophylactic neck dissection in patients with locally controlled cancer of the oral cavity (with the exception of the lip) is not agreed upon. In spite of a mass of statistical evidence that prophylactic neck dissection would serve no useful purpose,[2] a large series of cases to demonstrate this positively has not been reported except in the case of the lip where the disease is more benign. There is no method of determining preoperatively whether cancer is present in lymph nodes that are not palpable, especially in the deep cervical region where cancer of the tongue usually metastasizes first. In order to remove nonpalpable cancerous lymph nodes, prophylactic neck dissection must be done. In the 1 case referred to above, penetration of the lymph node capsule by cancer cells was observed in a neck dissection specimen removed prophylactically. Further observations and trials of this plan are necessary before any conclusions can be drawn.

SUMMARY

1. Detailed pathologic studies were made on thirty-nine specimens from cervical lymph node dissections on thirty-three patients.

2. The lymph nodes in all specimens were recorded as to total number and location. The suprahyoid area contained an average of eight lymph nodes per specimen and infrahyoid area thirty-six lymph nodes per specimen. The largest single radical neck dissection specimen contained 146 nodes.

3. It was found that this type of tissue was not suitable for use of clearing methods as employed by Gilchrist and David.[1]

4. Analysis of the spread of tumor indicated that penetration of the lymph node capsule by tumor cells influenced the prognosis less than the known long duration of cervical metastases and the position or surgical accessibility of the lymph nodes. This was especially true of carcinoma of the tongue.

5. The early insidious spread of squamous cell carcinoma of the oral cavity, especially from the tongue, is perhaps best treated by prophylactic neck dissection in patients who may be expected to survive the operative procedure.*

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The authors are grateful for aid in clearing specimens rendered by Dr. O. V. Batson, Professor of Anatomy, Graduate School of Medicine, University of Pennsylvania, and to the residents in Surgical Pathology who performed many of the lymph node studies.

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* For discussion see page 802.

THE ROENTGENOLOGIC DIAGNOSIS AND FOLLOW-UP OF HYPOPHARYNGEAL CANCER*

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IN SWEDEN the hypopharynx is a relatively common site for cancer, and 60 per cent of our patients are women. Compared with other countries, it is a rather high percentage of women. In France and Switzerland, for example, cancer of the hypopharynx is very rare.

In the term hypopharyngeal cancer we include all cancers from the valleculae to the upper part of the esophagus, except the intrinsic laryngeal cancers.

Thus, the tumors originating at the junction of the hypopharynx and the esophagus, at the level of the sixth cervical vertebra, are also classified as hypopharyngeal cancer. Therefore, we differentiate between cancer of the upper and cancer of the lower portion of the hypopharynx, and the borderline between these two groups is drawn at the superior border of the cricoid cartilage.

In the presence of tumors involving the upper portion of the hypopharynx, the chief purpose of roentgen examination is to supplement the laryngoscopic examination by furnishing information as to the lower limit and the depth of the already diagnosed tumor.

In the presence of deeply situated tumors in the region of the entrance to the esophagus, the purpose of the roentgen examination is to establish at the earliest possible stage evidence of any change of the wall and to assist in establishing its nature. This is an achievement which, from the roentgenological point of view, and as far as its value is concerned, is comparable to any roentgenologic demonstration of a malignant tumor anywhere else in the alimentary tract.

An essential prerequisite for a correct interpretation of the tumor changes, especially the early ones, is an intimate knowledge of the rather complicated normal roentgenologic appearance in this region.

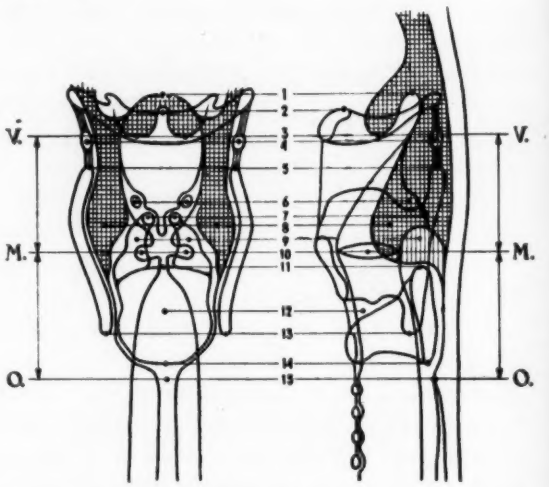

FIG. 1. Schematic diagram of the larynx and pharynx with planes of orientation.
V = Vallecula plane, M = Morgagni plane,
O = Esophageal Opening plane.
1 = Superior border of the epiglottis.
2 = Superior border of the hyoid bone.
3 = Bottom of the valleculae epiglotticae.
4 = Triticeous cartilage.
5 = Apex of the cornu superior of the thyroid cartilage.
6 = Cuneiform tubercle (Wrisbergii).
7 = Corniculate tubercle (Santorini).
8 = Recessus pyriformis.
9 = Region of the arytenoid cartilage.
10 = Ventriculus laryngis Morgagni.
11 = Superior border of the signet plate of the cricoid cartilage.
12 = Subglottic laryngeal cavity.
13 = Apex of the cornu inferior of the thyroid cartilage.
14 = Inferior border of the signet plate of the cricoid cartilage.
15 = Esophageal opening (Killian's "mouth of the esophagus").

* Presented in a Symposium on the Head and Neck at the Thirty-third Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–9, 1951.

The analysis of the roentgenological findings in pathological cases will be made with greater ease if certain previously determined planes are marked both on posteroanterior and lateral views. On comparing the two views for the purpose of closer study of a certain detail, these previously determined planes will greatly facilitate orientation.

For this purpose, we have chosen three different auxiliary planes which all have one thing in common: they are usually very clearly visualized or can be constructed in both posteroanterior and lateral views. The three auxiliary planes which are shown on the drawings (Fig. 1) illustrating the normal roentgenological appearance are the following.

1. The vallecula plane through the bottom of the valleculae—V-plane.

2. The Morgagni plane through the ventricle of the larynx—M-plane.

3. The esophageal opening plane through the junction between the pharynx and the esophagus—O-plane.

If one of the views discloses a suspicious detail at a certain level, one immediately knows at which level the same detail may be found in the other projection.

The essential of the roentgenological technique is that besides the usual soft tissue roentgenograms we take films after ingestion of an opaque medium, some showing the mucous membrane in posteroanterior, oblique and lateral positions, and some showing the hypopharynx completely filled. Through the contrast medium we get a much more precise idea of the appearance and the topographical extent of the tumor than on the soft tissue roentgenograms.

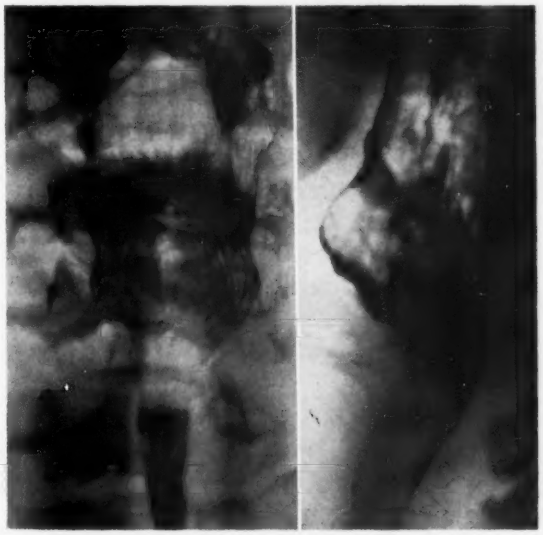

Fig. 2. Posteroanterior and lateral views illustrating the normal mucosal folds.

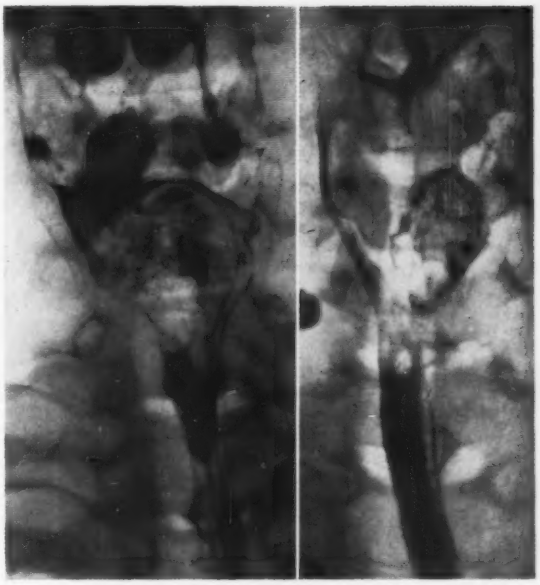

Fig. 3. Cases with pathologic postcricoid mucosal pattern of neoplastic origin.

On the relief films we get a good view of the mucous membrane. They must be carefully analyzed, and even the slightest deviation from the normal should be considered and evaluated, especially if it is brought out in both posteroanterior and lateral views.

Figure 2 shows a normal relief film with valleculae, aryepiglottic folds, pyriform fossae and the fine, concentric mucous membrane folds in the postcricoid region, contrasting with the parallel folds in the esophagus.

With small tumors in the postcricoid region we only get an abnormal pattern (Fig. 3). Since the prevertebral shadow is of normal thickness in such early cases, only the relief view can give us the roentgenological diagnosis.

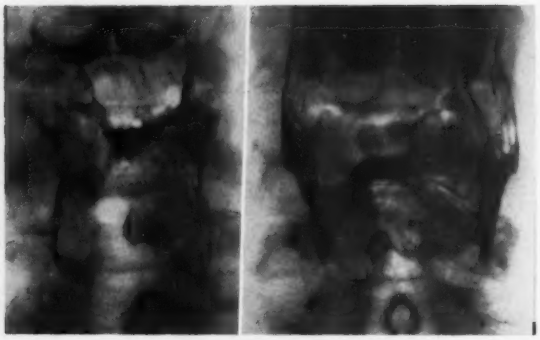

FIG. 4. *Left*, a pathological broadening of the right aryepiglottic fold; *right*, a pathological enlargement of the left arytenoid region.

If the tumors are localized more cranially, we sometimes can get an enlargement of the arytenoid region or a broadening of the aryepiglottic folds, as Figure 4 shows.

In every case with the slightest dysphagia, we must also take roentgenograms with maximal filling of the hypopharynx and the upper part of the esophagus (Fig. 5). These films should be exposed immediately after the patient is told to swallow. Upon the command of the roentgenologist, the patient must swallow as large a quantity of opaque medium as possible in one single bolus. When practicing this "swallowing by command," the roentgenologist should count aloud from 1 to 4. At "3" the patient should swallow, and at "4" the assistant should make the exposure. This simple procedure enables both partners to accurately time the moment of action.

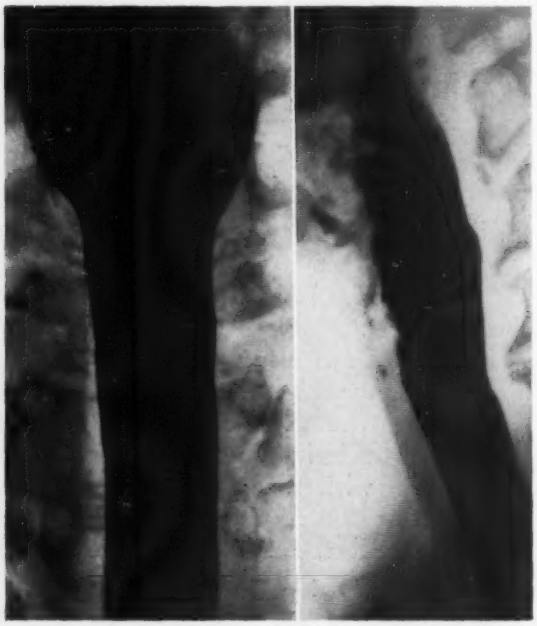

FIG. 5. Posteroanterior and lateral views of a maximal filling of the hypopharynx and the upper part of the esophagus (normal case).

FIG. 6. Small valvular strictures in a patient with the Plummer-Vinson syndrome, seen only on the lateral view.

This is the only method with which we can obtain the typical valvular strictures of the Plummer-Vinson syndrome, which in Sweden is a cancer-predisposing disease of great importance. Sometimes very small valvular strictures can be seen only on the lateral view (Fig. 6); sometimes we see very severe strictures in the upper part of the esophagus with dilatation above them (Fig. 7).

When we have diagnosed a Plummer-Vinson syndrome, the patient comes back every six months for follow-up examination. If she feels worse, she is told to come back at once. Through those regular control examinations we have been able to

diagnose carcinomas before they have caused any new symptoms.

The following case may be cited as an example:

The patient, a woman, aged sixty, was, in November, 1943, referred to the roentgen department because of dysphagia. The roentgenograms showed typical valvular strictures (Fig. 7). By a control examination in 1948 a marginal defect was seen on the posterior wall (Fig. 8). We were suspicious of a tumor but the biopsy showed only precancerous changes. The follow-

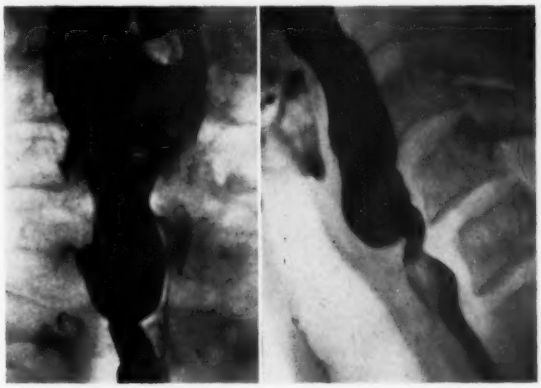

Fig. 7. Typical severe strictures in the upper part of the esophagus, in a woman aged sixty.

up examinations were now made at shorter intervals and in March, 1950 (Fig. 9), a large tumor was found in the right aryepiglottic fold. At that time the biopsy showed cancer. The patient's symptoms had been unchanged during the entire period.

We have many cases of this type, and in every case the tumor has arisen above the valvular strictures, showing that the whole mucous membrane and not only the place for the strictures is affected.

When we have diagnosed a carcinoma of the hypopharynx, we indicate the tumor for the clinicians to reveal the extent of the tumor and to demonstrate the degree of invasion by the tumor into the normal surrounding tissues. For this we use special centimeter scale skin markers (Fig. 10). Through this method the clinicians can decide the exact fields and the tumor dose which the clinicians consider most important.

Fig. 8. The same patient five years later. No valvular strictures but a small marginal defect on the posterior wall.

Fig. 9. The same patient after an additional two years. Now there is a large malignant tumor in the aryepiglottic fold.

FIG. 10. Posteroanterior and lateral views illustrating the technique of indicating the extent of the tumor.

At the Radiumhemmet cross-fire technique with four fields is used: one anterior and one posterior on each side of the neck. The fields are rather narrow, 3.5 to 4 cm., but extend in most cases from the edge of the lower jaw down to, or often several centimeters below, the clavicle.

The clinicians have found that the total tumor dose required to produce a complete regression of the tumor is about 5,700 to 6,000 roentgens given over a period of about one month. To achieve this, each field receives 2,600 to 3,000 r.

Two to four weeks after the roentgen treatment has started, a reaction commences and on the roentgenograms we can see a decrease in the prevertebral soft tissue shadow and the mucous membrane becomes smoother, at first due to edematous swelling.

An atrophy of the mucous membrane appears later. This gives such a typical roentgenogram (Fig. 11) that we can immediately tell if a patient has had roentgen therapy. All irregularities as well as the mucosal folds are smoothed out and slippery so that the opaque medium does not adhere in the usual manner to the mucous membrane. The lumen appears to be rigid and deficient in elasticity during the act of swallowing.

Besides this initial reaction, we have, however, established a later change which must be considered in direct connection with the radiation treatment received. As the picture is strongly suggestive of that of a local recurrence, it is of the greatest importance to recognize this secondary reaction.

In many cases we have seen that the prevertebral soft tissue shadow has again increased in width and the outline of the mucous membrane has again become ragged. All the changes have, however, regressed without any further roentgen treatment, and biopsies have only shown necrotic mucous membrane tissue and edema.

The following case may exemplify this late reaction:

A woman, aged forty, was referred because of dysphagia. On examination in October, 1948, we found a large tumor with pathological broadening of the prevertebral soft tissue

shadow and with irregularity and stenosis for 6 cm. in the postcricoid region (Fig. 12).

One month after roentgen treatment the prevertebral soft tissue shadow had decreased markedly and the examination with contrast medium showed an atrophy of the mucous membrane in the affected region (Fig. 13).

The routine examination three months later showed that the prevertebral soft tissue shadow

Fig. 11. Typical appearance of the hypopharynx after radiation treatment.

remained the same but an irregularity was seen on the anterior wall of the postcricoid region (Fig. 14). Naturally, in such a case we may suspect a recurrence but as the changes were confined to the mucous membrane we had also to think of late changes due to the therapy, and the biopsy showed in this case only necrotic tissue without cancer.

The roentgenogram (Fig. 15) from an examination two months later without further

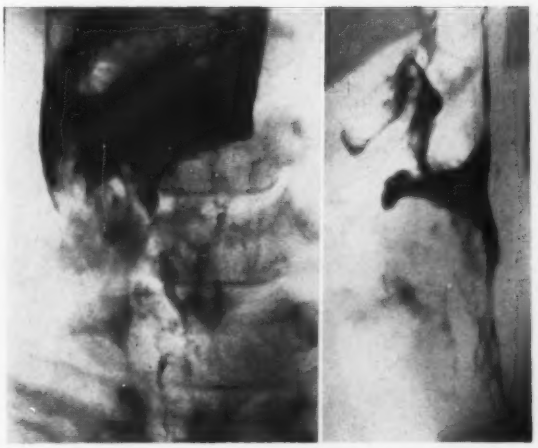

Fig. 12. Large tumor in the postcricoid part of the hypopharynx with pathological broadening of the prevertebral soft tissue shadow and with irregularity and stenosis.

roentgen treatment showed that the prevertebral soft tissue shadow had further decreased. The previously noted irregularity had also disappeared.

The explanation of these changes should probably be sought in a late reaction after irradiation or they should be considered

Fig. 13. Same patient one month after roentgen treatment, showing decreased width of the prevertebral soft tissue shadow and atrophy of the mucous membrane.

FIG. 14 FIG. 15

FIG. 14. Same patient after an additional three months. Again irregularity on the anterior wall, typical late reaction.

FIG. 15. Same patient after an interval of two more months. The irregularity has now disappeared without further roentgen treatment.

as an expression of the reaction of the irradiated tissue to some extrinsic factor, for example an infection.

The time between irradiation and the first appearance of the changes described has varied considerably. In some cases they appear as early as three months after roentgen therapy; the longest interval was eleven months and thus no guidance to a correct diagnosis is afforded. Commonly the changes have regressed during some months without any treatment.

This late reaction is much more common than we had thought earlier. This we can establish now since we have done systematic investigations at short intervals. We have not been able to decide if there is any difference in the treatment of these patients with late reaction and the remainder of the patients, which could explain these changes.

It is, however, important to bear in mind the possibility of late reactions in the evaluation of the prognosis and to suggest in cases of a suspected recurrence a direct hypopharyngoscopy with biopsy.

Earlier, undoubtedly, a number of such "false recurrences" have been treated again with roentgen radiation, resulting in a fatal necrotic disintegration.

The five year cure rate in cases of carcinoma of the hypopharynx at Radiumhemmet has increased from 5 per cent to 17 per cent and the palliative effect is also much greater. At present, one year after treatment 32 per cent of our cases are free from signs and symptoms of disease, but ten years ago our one year cure rate was reported as only 16 per cent.

We are of the opinion that some of the factors responsible for this improvement are early roentgen diagnosis, carefully localized treatment fields, and the recognition of the late reactions.

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DISCUSSION OF SYMPOSIUM ON THE HEAD AND NECK

PAPERS OF DRS. CASTIGLIANO AND ROMINGER, EBERHARD, ROYSTER ET AL., AND WELIN

DR. WILLIAM S. MACCOMB, Houston, Texas. Dr. Castigliano's work has been admirably presented. In the early days at Memorial Hospital most of the therapy was by irradiation, either by interstitial or external, or combination of methods. Such treatment often resulted in necrotic ulcers. Later we found it necessary to attempt surgical removal of these ulcers. Very often the ulceration was not due to irradiation only, but also to reactivity of the disease.

Dr. Royster's paper, in which he shows the actual number of nodes involved with the early invasion of the capsule, is extremely interesting and important. A careful survey by the pathologist of all tissues removed is a great help to the surgeon in evaluating the prognosis.

DR. CHARLES L. MARTIN, Dallas Texas. Since our method of treating metastatic cervical lymph nodes with low intensity radium needles plus roentgen therapy has been referred to, I feel that I should enter this discussion. I would like to emphasize the fact that this pro-

cedure does not produce sloughs requiring subsequent surgery when it is carried out properly and the five year salvage rate is comparable to that produced by block dissection.

It is my impression that the doses of radiation given by Dr. Castigliano as a preoperative measure are well below those needed to cure squamous cell carcinoma in lymph nodes. If so, such an elaborate procedure seems hardly justified when it is to be followed by radical surgery. You may be interested to know that a block dissection can be carried out in a neck which has been subjected to our rather radical technique and we are now resorting to surgery in an effort to produce a cure in some of our cases which have not been completely controlled.

With Dr. Castigliano's technique, treatment is administered to multiple small portals. The lymph nodes are connected by a dense network of lymphatics and it seems quite possible that malignant cells might be located between his portals and not receive any radiation at all. We have attempted to cover a whole section of the neck with our technique in an effort to treat all the malignant cells in the involved area.

If I may, I would also like to discusss Dr. Eberhard's paper. He apparently shares the opinion of many others that the proper implantation of radium needles is a difficult procedure. It is true that the work requires some experience but any physician who has had an internship can master the technique under proper supervision in a relatively short time.

The implantation should not be followed by severe pain or infection and most of our patients are up and about and able to eat soft and liquid food on the second day in the hospital. I cannot end this discussion without restating my firm belief that low intensity radium needles provide the best method of treatment now available for intraoral carcinoma.

Dr. Maurice Lenz, New York, New York. Dr. Eberhard's comments on the good results of interstitial irradiation in cancer of the anterior two-thirds of the tongue are timely, especially in view of the present tendency to treat all these cases by surgery. The value of interstitial radium treatment in this location was supported by the reports presented at the 1948 meeting of this Society. These reports comprised the five year results in close to 3,000 similar cases. Dr. Eberhard has pointed out that radionecrosis is less likely, when the position of the needles is controlled roentgenographically after insertion. He has also emphasized the superiority of low, as compared to high intensity needles, a fact which is often stressed by Dr. Charles Martin.

Dr. Eberhard should be commended for his presentation.

Dr. Milford D. Schulz, Boston, Massachusetts. While we are on the matter of placement of radium needles, I should just like to carry the digression a little bit further.

Next week, at the meeting of the American Medical Association, Dr. Robbins, and Dr. Land of the Polaroid Corporation of Boston, are going to present an exhibit and a paper dealing with the Land Polaroid method of rapid film processing for medical roentgen diagnosis. I should like to call your attention to the usefulness of this method as a means of checking upon the accuracy of the placement of radium needles, inserted interstitially into tumor-bearing areas.

I think everyone must be familiar with this Land Polaroid camera which is on the market. By this method, a dry print showing the needle implantation can be had within one minute, thus enabling the therapist to be sure immediately that his needles are where he wants them and to correct any deviations from his planned scheme before the effects of the anesthesia have worn off and before the sterile technique has been broken. When check-up films, which everyone admits are desirable, are delayed until after the patient has left the operating room, there is sometimes a tendency to accept implantations which are less than ideal. The ready availability and the rapidity with which this information is to be had by means of this method of examination will tend to obviate that occurrence.

Dr. Hugh F. Hare, Boston, Massachusetts. At this time, I should like to ask the essayists a few questions as I think there is, to a certain degree, a lack of uniformity so far as radiation treatment is concerned. One thing we have been told so many times is that we must avoid wet tissue reactions in delivering irradiation. It appeared that the film shown this morning gave evidence that the tissues, at least the skin tissues, received a wet desquamation; the healing was not that shown when radiation is given so that the wet tissue reactions do not occur.

Would the essayists in discussing their papers

be willing to give their half-value layers and, also, the daily tumor dose delivered?

DR. CASTIGLIANO (closing). I do not have an axe to grind, either surgical or radiological. Dr. Martin did misunderstand me.

Many surgeons and radiologists have believed that radical neck dissection is not a technically feasible procedure if attempted after intensive roentgen irradiation has been delivered to the neck. It has been strongly believed that after intensive irradiation extensive operations are technically exceedingly difficult, if not impossible, to perform, and, if performed, the risk of serious complications and death is great.

All I have tried to do in a small way is to test the *correctness* of this belief. Today we strongly believe that in properly selected cases waging a control action on the neck metastasis while destroying the primary lesion, followed by radical neck dissection, is a safe procedure if the recommendations of this paper are followed. Although we are not prepared to say so, we feel that the method herein described will be productive of better results for those enthusiastic enough and willing enough to take the time to combine precision irradiation techniques with radical cervical surgery.

When neck metastasis is inoperable, we then favor irradiation, employing combined roentgen irradiation and low intensity gamma irradiation, as offering the best chance for long-term palliation.

In answer to the question regarding dosage, the average dose delivered to the cervical metastasis was 5,300 r. The high dose was in excess of 11,000 r. The average time to deliver the dose was thirty-eight days.

In answer to the question dealing with skin reaction, we achieved an ulcerative reaction in every case where we started the treatment to the cervical metastasis early enough to deliver sufficient irradiation.

The daily dose was 300 r (in air) to each portal. If we had three foci of metastasis, we treated with three portals shaped to fit the metastatic mass and a small zone of apparently normal tissue. As the mass decreased in size, the portal was decreased in size.

The average *complete* healing time of neck dissections in cases receiving intensive irradiation required thirty-eight days as compared with twenty-seven days in the nonirradiated cases.

If the neck portals are not over a total of 60 sq. cm. and the doses between 4,000 and 6,000 r (in air), a radical neck dissection is a perfectly feasible procedure.

I believe that irradiation methods alone are too conservative an approach for the management of so deadly a condition as is cervical metastasis.

I should like to close this discussion by repeating the final sentence of the formal paper to be published. There is no reason to believe that cervical lymph node metastasis should not be managed as radically as is consistent with fundamental oncologic concepts as practiced in other areas of the body afflicted with cancer.

DR. EBERHARD (closing). I am afraid Dr. Martin misunderstood me too. My purpose was to prove that he was right. Low intensity is certainly much to be preferred from most aspects. I do disagree with him that implantation of the tongue with needles is easy. I am just simply confessing how clumsy I am and how many years it has taken me to learn to do it even halfway right—I know he can do it much better.

I also must disagree with him that these patients wander around the hospital for a week perfectly happy. I have a little trouble controlling some of these patients; they are not in pain but they are most uncomfortable.

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PARAMETRIAL INJECTION OF COLLOIDAL GOLD (Au^{198}) IN THE MONKEY*

By J. F. NOLAN, M.D., E. G. JONES, M.D., *and* R. H. NEIL, A.B.
LOS ANGELES, CALIFORNIA

THE present study represents a continuation of previous experiments designed to evaluate the adaptability of radiogold to the problems presented in the treatment of carcinoma of the uterine cervix.[11] Failures of conventional methods of treatment in this disease have been attributed to inadequacy of dosage to lateral parametrial extensions and lymphatic metastases in the pelvic lymph nodes. The usual means of radiation therapy may fail primarily because of low dosage to the lateral pelvis, or, secondarily, because of overdosage to the parametrial triangle in an attempt to increase the dose at the lateral pelvis.[1] Whether metastatic carcinoma in the pelvic lymph nodes may be destroyed by radiation methods or is peculiarly resistant to this therapeutic means is still a moot point. However, there is strong suggestive evidence that irradiation of these areas is a worthwhile procedure in terms of five year survivals of patients.[9] Surgical removal of primary lymph nodes in carcinoma of the uterine cervix results in about a 20 per cent five year survival rate if lymph nodes are involved.[7] The technique of surgical extirpation is difficult and many times inadequate because of the anatomic relationships among the lymph node bearing tissues, the large vessels, and the ureter. It is believed that the physical, chemical, and biologic characteristics of radiogold lend themselves peculiarly to the attack upon this phase of the problem of treatment of carcinoma of the uterine cervix.[2]

Physically, the radioactive element is Au^{198}, which is characterized by a short half-life (2.7 days) and two radioactive decay schemes. These result in the liberation of beta rays of 0.97 mev. peak energy in 85 per cent of the nuclei and of 0.61 mev. peak energy in the remainder. The nuclei which liberate the lower energy beta rays then emit energy in the form of two gamma rays in cascade (0.21 mev. and 0.157 mev.). All the nuclei then emit a gamma ray of 0.41 mev. to return to a stable state as Hg^{198}.

Most of the biologic reaction is the result of the beta radiation which has a half range of about 0.8 mm. in tissue. Owing to this short range of the beta particles the ionization is limited to the region in which the element is contained. The additional gamma rays add to the range of biologic reaction, but probably account for only about 10 per cent of it.

Chemically, the material is in the form of a colloid which is composed of very small particles; namely, 0.003 micron. In these experiments, the colloid† was mixed with a 1 per cent pectin solution as a further suspending agent to bring it to the proper dilutions.

Biologically, the particulate material is phagocytosed by cells of the histiocyte series and carried along lymphatic channels to lymph nodes and to the general reticuloendothelial system.

The previous studies mentioned have shown that the material can destroy transplanted squamous cell carcinoma in mice; that when injected in the parametria of rabbits it proceeds to the lymphatic structures in the pelvis and the primary lymph nodes; and that the tolerance levels, as far as necrosis is concerned, are well above the practical and theoretical cancerocidal doses. In addition, the colloid, in tracer

† Obtained from the Abbott Laboratories.

* From the Albert Soiland Cancer Foundation, Los Angeles; the Los Angeles County General Hospital, and the University of Southern California, Department of Obstetrics and Gynecology. Presented at the Thirty-third Annual Meeting, American Radium Society, Atlantic City, N. J., June 7–9, 1951.

TABLE I

EXPERIMENTAL INJECTION OF COLLOIDAL RADIOGOLD

Time		Monkey		Parametrium				Breast				Total	
Active days	Half-lives	No.	kg.	Right		Left		Right		Left		mc.	cc.
				mc.	cc.	mc.	cc.	mc.	cc.	mc.	cc.		
—	—	525	2.5	—	—	—	—	—	—	—	—	—	—
—	—	577	2.6	—	—	—	—	—	—	—	—	—	—
—	—	452	2.4	—	—	—	—	—	—	—	—	—	—
2	0.8	432	2.4	3.0	2.0	3.0	2.0	—	—	—	—	6.0	4.0
3	1.1	591	2.6	10.0	2.5	—	—	—	—	—	—	10.0	2.5
5	1.8	441	2.6	3.0	2.0	3.0	2.0	—	—	—	—	6.0	4.0
6	2.2	949	2.2	18.0	4.5	—	—	—	—	—	—	18 0	4.5
6	2.2	413	2.7	3.0	2.0	3.0	2.0	—	—	—	—	6.0	4.0
6	2.2	445	2.3	4.5	1.0	4.5	1.0	—	—	—	—	9.0	2.0
10	4.0	412	3.0	3.0	2.0	3.0	2.0	—	—	—	—	6.0	4.0
11	4.1	057	2.5	10.0	2.0	10.0	2.0	—	—	—	—	20.0	4.0
13	4.8	600	3.3	20.0	5.0	—	—	—	—	—	—	20.0	5.0
14	5.2	490	2.2	4.5	1.0	4.5	1.0	—	—	—	—	9.0	2.0
15	5.5	150	2.3	5.0	4.0	—	—	—	—	—	—	5.0	4.0
15	5.5	032	2.8	10.0	4.0	—	—	—	—	—	—	10.0	4.0
15	5.5	323	1.9	—	—	—	—	—	—	20.0	4.0	20.0	4.0
17	6.3	576	2.3	20.0	6.0	20.0	6.0	—	—	—	—	40.0	12.0
17	6.6	543	2.9	11.0	3.0	11.0	3.0	—	—	—	—	22.0	6.0
19	7.0	206	4.5	10.0	2.0	10.0	2.0	—	—	—	—	20.0	4.0
20	7.2	324	3.5	28.0	7.0	—	—	—	—	—	—	28.0	7.0
24	9.0	446	2.2	4.5	1.0	4.5	1.0	—	—	—	—	9.0	2.0
26	9.7	434	2.0	10.0	2.0	10.0	2.0	—	—	—	—	20.0	4.0
—	—	451	2.8	4.5	1.0	4.5	1.0	—	—	—	—	9.0	2.0
28	10.5	221	3.7	10.0	2.0	10.0	2.0	—	—	—	—	20.0	4.0
31	11.4	131	3.0	20.0	4.0	—	—	—	—	—	—	20.0	4.0
31	11.4	318	2.5	—	—	—	—	20.0	4.0	—	—	20.0	4.0
34	12.6	812	1.4	0.29	1.0	—	—	—	—	0.29	1.0	0.58	2.0
34	12.6	905	2.3	0.58	2.0	—	—	—	—	0.29	1.0	0.87	3.0
34	12.6	928	2.6	1.16	4.0	—	—	—	—	0.29	1.0	1.45	t.0
41	15.2	911	2.4	1.50	1.0	1.50	1.0	—	—	1.50	1.0	4.50	3.0
41	15.2	748	2.0	3.00	2.0	—	—	—	—	1.50	1.0	4.50	3.0
41	15.2	703	3.0	6.00	4.0	—	—	—	—	1.50	1.0	7.50	4.0

amounts, has been injected into the parametria of human beings per vaginam.[12] It has been demonstrated in the pelvic lymph nodes at subsequent operation. The present study was designed to explore the general and local tolerance levels for radioactive colloidal gold injected into the parametrium.

PROCEDURE

The *Macacus rhesus* monkey was used as a test animal because of its anatomic similarity to the human subject.[4] After anesthesia by intravenous nembutal, the animals were subjected to celiotomy and the pelvic organs exposed. Injections were made between the leaves of the broad ligament by introducing a small bore hypodermic needle between the round ligament and the tube, and passing it downward to the level of the internal os of the uterus. The solution was injected slowly in order to avoid too rapid distention of the tissues, which might cause rupture of the thin layers of peritoneum and subsequent peritoneal spill of the material. After injection, the laparotomy incision was closed and dressings were applied.

Average readings on the back of the hand of the operator were measured with a small Beckman ion chamber. These were about 0.1 milliroentgen per millicurie. per minute. This rate of irradiation was found to be about the same

as that received by the operator in the performance of an interstitial needle implantation or application of radium capsules in a sponge rubber colpostat in the treatment of carcinoma of the cervix. However, the dosage rate was twice that involved in the application of radium as a tandem or with the Ernst applicator. However, the time involved in making the actual injections of radiogold was rather short (one to two minutes).

At various intervals the animals were sacrificed by intracardiac injection of air, and necropsied. The gross appearance of the peritoneal contents was noted and various organs were removed for radiochemical and histologic study.

Table 1 shows the various experiments carried out as far as the amount of material, site of injection, and time of sacrifice were concerned. The total number of experiments was small, but an attempt was made to diversify the injections in order to gain as much information as possible from each animal. Rather massive doses were used in order to produce intense local reactions and general toxicity, if possible. Total doses ranged from 0.58 to 40 millicuries, and individual parametrial injections varied from 0.29 to 28 millicuries. The times of sacrifice varied from two to forty-one days, or about 0.5 to 11 half-lives. One animal is still being maintained alive and apparently healthy, over three months after injection of 9 millicuries of the material.

GENERAL REACTIONS

One of the problems investigated was the general toxicity of the material to the animal. In order to do this, the removed organs were studied as far as distribution of the radiogold was concerned. The excised tissues were extracted, and the residual radioactivity measured after an acid hydrolysis and ashing technique, which will be described in a separate paper. The method involves dissolution of the tissues by boiling in concentrated hydrochloric acid, and absorption of the gold by a carbon carrier. Control tests with "blanks and spiked runs" have indicated at least a 97 per cent yield of the injected material by this method. Aliquot samples were plated and counted with the same thin-window Geiger-Müller counter and scaler.

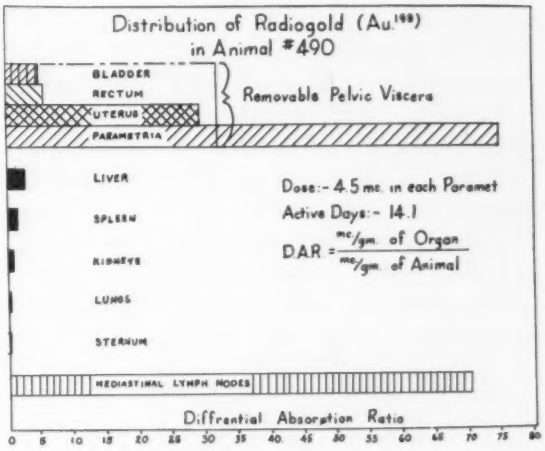

Fig. 1. Description in text.

Figure 1 shows the general distribution of the material in various organs of the same animal two weeks after injection. The amount of radiogold recovered is expressed as the differential absorption ratio (D.A.R.), which is a factor derived by the following formula: D.A.R. = millicurie per gram of organ divided by millicurie per gram of animal injected. In this expression the physical decay, amount of material injected, and weight of the test organ are all taken into account. The various organs examined showed a tendency for the material to remain in and around the site of injection, but there is measurable dispersion mainly to the organs rich in reticuloendothelial cells. Of these, the liver, spleen, and lymph nodes seem most important.

The bar graph shows that the amount of colloid which remains in the pelvis is about twenty-five times that in the liver. The material is mainly concentrated in the parametria. Actually, the whole block of pelvic tissues which were removed for study represent only 0.6 per cent of the weight of the animal, and the parametrial tissue comprises only one half of this. Included in the dissected parametria were pelvic lymph nodes which stripped from the large blood vessels; the secondary nodes in the periaortic regions were not included. The high concentration in the distant lymph nodes is remarkable, and probably

represents dispersion of the material through the thoracic duct.[6] Distribution studies of radioactive gold after tumor infiltration, intracardiac, intraperitoneal, and intrasplenic injection in smaller test animals have shown findings similar to these.[14]

Because of the large volume, high absorption ratio, and physiologic importance of the liver, it was taken as a test organ to explore the relationship of its absorption to that of the injected site. Figure 2 shows this comparison in relation to time after injection. The "site of injection" as described is represented by all of the removable pelvic viscera, including the rectum, uterus, vagina, bladder and parametria. A few of the animals were injected in the subareolar tissue of the breast in addition to the parametrial injection, and one figure represents breast injection alone. Also, one animal was injected with a massive volume (12 cc.) which infiltrated almost all of the retroperitoneal tissue in addition to the parametria.

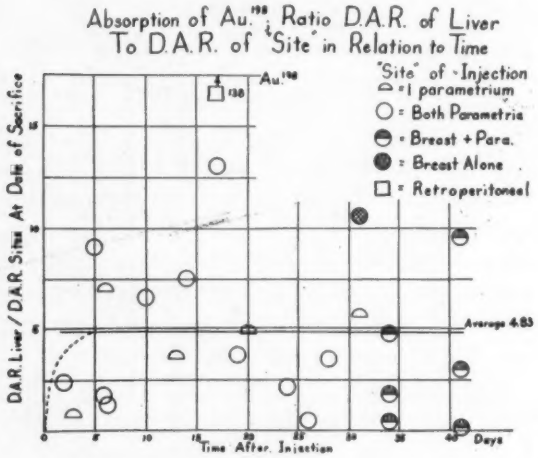

FIG. 2. Description in text.

The relation of the differential absorption ratios of the liver to the "site of injection" indicates that there is a fairly stable proportion of dispersion. With the usual doses, this ratio is about 5, although the high retroperitoneal injection and the large single dose in the breast showed a much higher percentage of the material in the liver.

The time element in the dispersion of the colloid from the parametrium is important because of the very short half-life of Au^{198}. Figure 3 shows this with curves for the differential absorption ratio of the pelvic viscera and for the liver in relation to time after injection. The amount remaining in the pelvis seems to drop rapidly and to become fixed within the first few days,

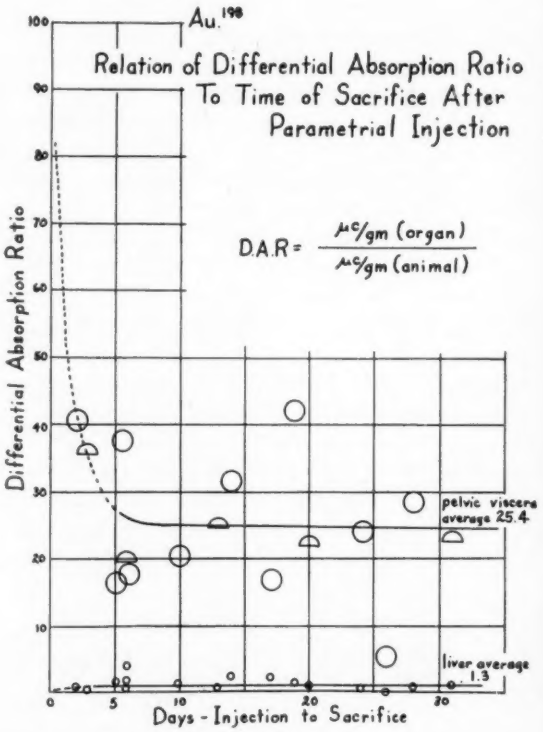

FIG. 3. Description in text.

while the amount reaching the liver rises from zero in a proportionately short time. It would be important to know whether this dispersion occurs in a matter of minutes, as it does from the general circulation,[10] or whether it is actually a matter of days because of the intensity of irradiation. Unfortunately, there are not enough animals in this series to pursue this point, but further studies are planned. Conversely, the amount of material remaining after 10 half-lives, or twenty-seven days, is not

important because only 0.3 per cent of the activity remains.

Despite the finding of measurable amounts of residual radioactivity in the liver after parametrial injection of radiogold, there were no evidences of impairment of function. Only one of the test animals died before the time scheduled for sacrifice, and this was found to have an infestation of intestinal worms. The others remained active and apparently healthy. Liver function tests, which included prothrombin time, cephalin flocculation, and thymol turbidity, were performed before injection and at the time of sacrifice in 14 animals subjected to doses of 6 to 50 millicuries, and sacrificed in from two to forty days. According to these studies, there was no demonstrable evidence of injury. The same tests were negative in the one living animal after seventy days. Furthermore, the histologic study of the livers revealed no evidence of destruction by the radiogold.

The absolute lymphocyte count was ascertained in 2 animals, ten and seventy days after injection. These counts were performed merely as checks and are certainly not conclusive, but they do suggest some lymphocytic suppression. The absolute lymphocyte count, after ten days, was 4,400 and, after seventy days, 4,800. The absolute lymphocyte count of a control animal living in the same conditions as the test animals, was 8,000. The blood counts of this control animal were within normal limitations as published for this species.[5] It seems logical that the high differential absorption ratio of distant lymph nodes should be reflected in such a reaction. However, histologic studies of the spleens, sternal bone marrow, kidneys and lungs, were similar to those of the livers in that no significant lesions were demonstrable.

LOCAL REACTION

As stated, the dosage levels in these experiments were purposely high in order to test the upper limits of tolerance. The gross appearance of the pelvic tissues was not remarkable. There were a few loose adhesions between the pelvic organs and the omentum in many instances, but no more than would be expected after a simple laparotomy incision. The retroperitoneal tissues were pigmented with the colloid, and oftentimes were fairly dense. In no instance was there gross evidence of hydroureter from compression or injury. There was no evidence of fistula, of hemorrhage,

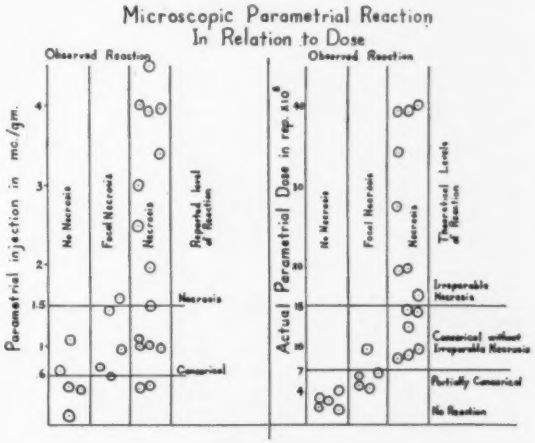

Fig. 4. Description in text.

or of rupture of the large blood vessel walls.

Microscopically, however, the reactions to doses of the higher levels were most intense. Figure 4 shows graphically the relationship between dose and histopathologic necrosis. It can be noted that doses in the order of 1.5 millicuries per gram of parametrium, or higher, show extensive injury with necrotic areas beyond repair in nearly all instances. Injections between 0.6 and 1.5 millicuries per gram showed necrosis in 5 cases, only focal necrosis in 5 cases, and no necrosis in 2 cases out of 12. These figures correspond roughly to findings reported for the rabbit parametrium. If there were 100 per cent fixation of the injected material, with complete decay the value of 0.6 millicurie per gram would correspond to about 50,000 rep per gram. Hahn has stated that this dose is about what may be expected to be cancerocidal for colloidal gold and raises

the question that our concepts of dosage must be readjusted.[3] Figure 4 also presents the histopathologic reactions in relation to actual doses measured in these experiments. These are compared to theoretical levels of reaction for roentgen and gamma rays, and this comparison is much closer. The discrepancy may well be due to the fact that there is uneven distribution of the

FIG. 5. Photograph of pelvic viscera in situ. Discoloration of retroperitoneal tissues seventeen days after parametrial injection of 12 cc. (40 mc.). Congestion of uterine corpus. Ovaries, bladder and rectum appear normal.

colloidal gold within the tissues of the parametria.

The colloidal particles seem to diffuse through the parametria along tissue planes or lymphatic channels, and can pass over to the uninjected side when only one parametrium is injected with a large volume. With small doses in the loose, fatty connective tissue of the parametria, there is often a peculiar reaction in the fat cells in which they appear immature. This may be a response from partial destruction. Generally, the material is localized in the periph-

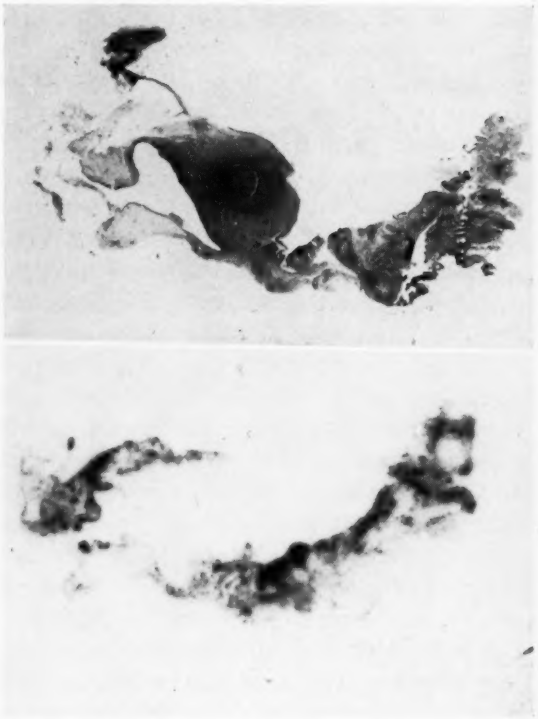

FIG. 6. Very low power section and radioautograph of uterus and parametria, showing concentration of radioactivity in parametrial tissues.

ery of the pelvic organs and can cause very intense reaction without much change in the epithelial layers. Radioautographs from microscopic sections demonstrated this localization in the peripheral tissues of the uterus, rectum and bladder. In very large

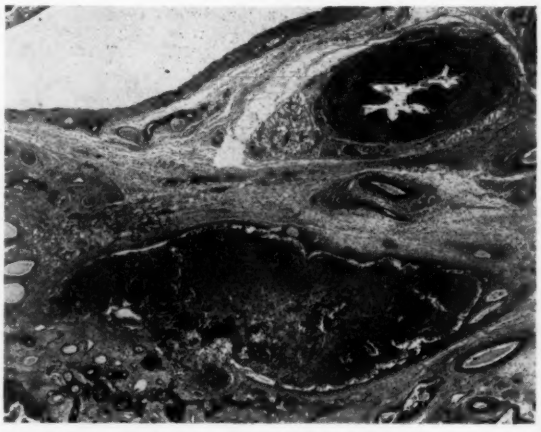

FIG. 7. Low power view of parametrium, showing ureter in upper right; extensive area of necrosis at lower left, and large lymph node with hilar thrombosis and necrosis in center of field.

doses (10 mc. or above) the material may almost completely destroy the supportative tissue or even the muscular layers of the ureters and large blood vessels. In many instances, it seemed remarkable that these tissues remained functioning and that their continuity was not disrupted.

Sections studied under the dark field, after microincineration, demonstrate the vivid yellow colloidal particles in the lymphatics and lymph nodes. With smaller doses, the lymph nodes would oftentimes be only partially destroyed in a segmental fashion. In larger doses, there were often great lakes of hyalinized material which represented completely obliterated lymph nodes, as "ghosts."

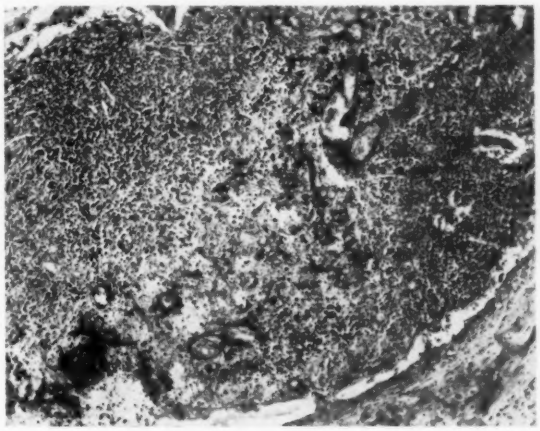

Fig. 8. High power view of same lymph node as shown in Figure 7.

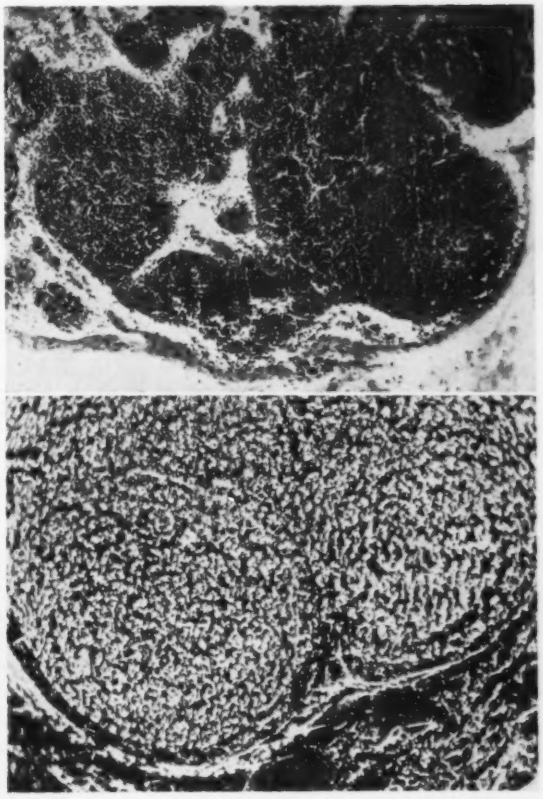

Fig. 9. Low power view of stained section and microincinerated section of lymph node, demonstrating distribution of radiogold throughout the substance of the node.

SUMMARY

The limitations imposed by necrosis of local tissues rather than liver injury seem to be the factors which should govern the the choice of dose which could be used in the human subject by a similar technique. To estimate tolerable limits for use of this material, a comparison may be drawn between the monkey and the human. Previous studies have indicated that transplanted cancers may be destroyed with doses in the order of 0.1 millicurie per gram of tumor tissue. This represents about 7,600 rep, which is a figure similar to the estimated cancerocidal dose in radium and roentgen therapy. The maximal tolerance dose, as based on local necrosis, may be some fifteen times this theoretical cancerocidal dose. It is probable that the intensity of radiation must approach the tolerance dose rather closely. Hahn has shown that not only are more intense treatments necessary with this material in advanced human cancers of large volume, but also such doses are well tolerated. This may be due to the short range of the beta activity in comparison to the size of the tumor from a volume concept. It seems likely that 25 to 50 millicuries in 50 cubic centimeters of solution could be injected into each parametrium of the human subject without difficulty This amount should diffuse uniformly through the volume of the parametria with enough of the material fixing in the local lymphatics and lymph nodes to cause sclerosis, without extensive necrosis, and

enough radiation intensity to be cancerocidal. Two important questions remain unanswered. These are: (1) Will the colloidal gold enter lymph nodes which contain metastatic cancer? and (2) If so, will the emitted radiation be cancerocidal to such metastases?*

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* For discussion see page 820.

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IRRADIATION OF CANCER OF THE UTERINE CERVIX WITH RADIOACTIVE COBALT 60 IN GUIDED ALUMINUM NEEDLES AND IN PLASTIC THREADS*†

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THIS is an interim progress report of the development of treatment methods evolved through the study of 100 cases of carcinoma of the endometrium, uterine cervix and a single case of vulvar carcinoma with vaginal extension. These cases have in common the use of cobalt 60 locally with free individualization of the application as a portion of their therapy. The report is limited by lack of five year survival statistics since the first case was treated less than three years ago. As confidence was gained in the efficiency of this method a more liberal selection of cases has been justified. According to best skill and judgment, the tumor area was irradiated to a predetermined roentgen dosage as uniformly as possible. Where tolerance to irradiation was limited by complications, previous irradiation or intercurrent disease, palliation of a specific distressing symptom was attempted.

MATERIAL

Carcinoma of the uterine cervix, grouped as follows into League of Nations clinical classification:

Clinical Stage 0— 2 cases
Clinical Stage I— 5 cases
Clinical Stage II—30 cases
Clinical Stage III—40 cases
Clinical Stage IV—17 cases

Adenocarcinoma of the endometrium—5 cases.
Carcinoma of vulva invading vagina—1 case.
20 of the above cases had had previous surgery.
33 are known to be dead at the time of this report.

METHODS OF TREATMENT

(1) *Uterine tandem and/or colpostat* (Paris type technique) used in cases of: (a) carcinoma of the endometrium preparatory to hysterectomy; (b) carcinoma of the uterine cervix where the disease is minimal or only local central palliation is indicated.

The cylinders used, 10 mm. long and 4 mm. in diameter, lend themselves readily to various loadings and distributions similar to radium. It must be remembered that the isodose curve about the ends of the cylinders is not as flat as with a radium capsule and allowance should be made for this in packing and spacing.

No complications were encountered with this method of application. Viable carcinoma was found to be present in the uterine horn of 1 of the 3 cases so treated in which the pathological material was available for study.

(2) *Multiple small sources* were packed into the uterine cavity in 2 cases of adenocarcinoma of the fundus.

(3) *Interstitial Needles.* Reference is made to previous reports for the methods of implantation, construction of interstitial needles containing small cobalt sources and calculation of dosage pattern.[1,2,4,7,8] These needles were inserted through lucite guides or templates or, in an occasional case, were implanted freehand.

Initially, cobanic cylinders 10 mm. long and 1 mm. in diameter were employed in stainless steel needles. Recovery of the radioactive material from this sheathing was so difficult that aluminum tubing was substituted for steel. Aluminum can be removed by dissolving it in a solution of

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5 per cent sodium hydroxide without sig nificant loss of cobalt if care is exercised. A desirably large tumor volume could not be implanted with sources of this linear intensity without unevenness of pattern due to separation of the needles and theoretically undesirable spacing between the sources within the needles.[9]

Twenty-six cases were treated with this style of radioactive source. Subsequently cobalt cylinders 3 mm. long and 0.5 mm. in diameter were used in aluminum needle sheaths which resulted in a smoother pattern. The external diameter of the needle was reduced from 2 mm. to 1.25 mm. resulting in less mechanical trauma.

(4) *Cobalt 60 in plastic tubing* was sewn into lymph nodes, bladder, urethra and vulvovaginal area where flexible applicators adapt well to tumor contour, minimize discomfort and reduce pressure necrosis. Details of technique are given in a previous paper.[7]

EVOLUTION OF THE LUCITE TEMPLATE

With increasing experience it became apparent that the desirable area to irradiate for carcinoma of the uterine cervix was a truncated pyramid with the base projecting into the wide parametrial areas. This is more or less in the vaginal axis and varies with uterine position and the palpable extension of the tumor either anteriorly or posteriorly. The need is apparent for a field of irradiation which is wider than the palpable tumor extension while a uniform dosage field must be maintained across the base of the diverging needles to avoid paracervical recurrence. The upper third or more of the vagina must be irradiated as a hollow tube to control any nonpalpable vaginal extension.

The guides were originally two or three plates with the inner plate usually perpendicular to the needle axis or face of the cervix as dictated by the anatomy of each case. Further experience indicated that the total area involved by contiguous extension could be reached through the vagina or translabially without unacceptable risk. A more recent innovation has been the use of a longer solid vaginal bougie which expedites the insertion of the needles, holds the vagina smooth for uniformity of surface irradiation thereby guarding against overdosage of the rectum which could infold between two separated plates. No complications have resulted from irradiation of the base of the bladder by a uniform dose. If the tumor appears to extend into the bladder or a need exists to irradiate behond the dorsal surface of the bladder, the guide is either depressed externally to secure the desired angle, while the bladder dome is elevated by a sound, or the bladder is deliberately transfixed.

The radiologist in the group has had misgivings relative to the departure from established custom by not irradiating the entire length of the uterine cavity in an early case. The clinician's concept, on the other hand, is well expressed in Davis's "Gynecology and Obstetrics"[3]: "As a rule, the cancer extends directly outward toward the pelvic wall. Rarely does it extend upward, even into the uterine cavity, except in the very late stages." A solitary experience with a recent case, however, suggests that the vascular and lymphatic boundary of the internal os is not impassable to vigorous tumors. Ostensibly this patient was a clinical Stage II despite known inadequate treatment elsewhere a year previously. Autopsy showed viable tumor cells in the fundus which in retrospect were indicated by positive Papanicolaou findings, although the cervix and broad ligaments were microscopically free of disease. Death occurred from massive pulmonary metastases.

The area above the internal os can be easily included by the use of a central tandem serving as a guide for the extended paracervical needles.

No special attempt has been made to prevent pyometria and only one case has occurred. This appeared early in the series before uniformity of dosage throughout

the pelvis was achieved. Dilatations of the cervical os have not been found necessary in the followup clinic.

THE COLPOCYSTOPROCTOGRAM AND CLINICAL EVALUATION OF CASE

Each patient with cancer of the uterine cervix receives initial external roentgen therapy to a tumor dose of 2,000 roentgens to the mid-pelvis, as soon as the diagnosis is established by biopsy. Factors are 250 kv. (peak), 15 ma., 50 cm. focus-skin distance, Thoraeus filtration equivalent to 3 mm. of copper, with a half-value layer of 3 mm. of copper, daily dosage of 200 r alternately to anterior and posterior portals 15 by 20 cm. angled down to include the vagina.

During this time an excretory urogram or retrograde pyelogram is made, together with cystoscopy, medical evaluation and any other indicated diagnostic examination.

Near the end of the course of therapy a combined visualization is made of the bladder outlined by liquid contrast material, the vagina distended with a soft rubber balloon or lamb's wool, and the lower colon with a thin barium enema. The lower bowel is simultaneously visualized by a dilute oral barium meal previously given. A suitable measuring device is included for calibration of dimensions distorted by the film. The outline of the vagina and the cervix is brightened by the addition of a small amount of radiopaque barium of proper consistency to be displaced by the vaginal balloon. The balloon is held in position by an obturator attached around the patient's waist. Stereoscopic anteroposterior and lateral films are made in the dorsal decubitus position, followed by laminagrams.

Concurrently a member of the gynecologic staff has made an independent manual and visual pelvis examination with careful measurement of the extent of the tumor, size of the vagina, and observation of any other pertinent findings. With the films available, a conference is held between the gynecologist, the physicist and the radiologist. The position, shape, and anatomical peculiarities of the individual patient are discussed and a diagram of the extent of the pelvic area to be irradiated is drawn, with consideration of the size of vaginal cuff to be treated, the amount of anterior and posterior extension of the tumor into the perametrium which must be included in the irradiation, the position and size of the uterus and cervix and of the normal structures to be avoided (bowel and bladder).

The choice of vaginal applicator is then made. Should the vagina not admit an obturator of sufficient size to carry the needles desired, a subpubic applicator is designed to fit the subpubic arch snugly and the needles are passed translabially. This usually occurs in late disease with adequate solid tumor to permit needle passage along the vaginal axis, and is employed frequently for palliation of far advanced disease, or closure of the vaginal opening to prevent exsanguination.

Roentgenographic examination has been found a useful complement to the clinical findings, since it gives visual aid to the physicist in designing the applicator, determines asymmetry and other peculiarities of the bladder, gives a permanent record of pre-treatment condition and serves to evaluate the positioning of the applicator during therapy.

The applicator is next designed and another pre-insertion conference is held to insure proper positioning of the needles or other problem of design for maximum efficiency of insertion. This latter conference must be attended by the individual who will be reponsible for insertion of the applicator. If the cervix is freely movable it is held in position by a small lucite centering rod projecting from the face of the plate or by transfixion of the cervix with silk sutures brought through or around the cervical face plate to prevent displacement of the cervix away from the applicator during insertion of the needles.

APPLICATION OF THE COBALT NEEDLES FOR CARCINOMA OF THE UTERINE CERVIX

The patient is prepared for surgery by inhibition of the intestinal flora with antibiotics.

The implantation is done in the lithotomy position with an indwelling catheter in the bladder.

The applicator is positioned against the cervix which can be seen through the clear lucite guide and is held in position by two or three metal rods threaded into the lucite template. More than one rod is desirable to prevent rotation of the implant and the holes serve as drains for the cervical face during the treatment period. Care is taken to ascertain the exact centering and depth of the implantation with due regard to the axis of the vagina and the patient. The cervix and vaginal mucosa are punctured by sharp pointed guides for a sufficient distance to insure free passage of the blunt aluminum needle containing the cobalt through the tissue. If the cobalt needle sheath is not too sharp it will deflect blood vessels and intestinal loops should they be encountered. The needle itself would control hemorrhage during the treatment period should a vessel be pierced. Roentgenograms are made during therapy to ascertain the position of the needles.

EFFECTS OF THE TREATMENT ON OTHER PELVIC ORGANS

1. *Bladder.* As indicated above, the bladder floor may be penetrated when necessary to adequately treat the tumor. Fears of exsanguinating hemorrhage, urine extravasation into the peritoneal cavity or fistula production have never materialized. No fistula can be attributed to dosages of 7,000 r accurately administered in this series. Five vesicovaginal fistulas have been encountered:

CASE I. D.S., an obese white woman, aged fifty-four, hypertensive, previously irradiated with a dosage of 2,400 r (in air) anteriorly and posteriorly to deliver maximum tolerable midpelvic dosage, followed by 5,000 r to each of two 3.5 cm. intravaginal portals aimed toward the parametrium for a clinical Stage III squamous cell carcinoma of the uterine cervix. Four months following one of the early implantations of cobalt, which did not include the anterior vaginal cuff, she developed a vesicovaginal fistula. Two months later the left ureter was transplanted to the skin and it was necessary at that time to ligate the right ureter because of local tumor involvement. Calculation of the dosage at the area of the fistula indicated that the bladder floor was not irradiated significantly by the cobalt.

CASE II. B.B., a white woman, aged forty-three, with chronic cystitis, squamous cell carcinoma of the cervix, clinical Stage IV. Eight months after cobalt implantation with one of the early incomplete patterns she developed severe vaginal pain and bleeding with a vesicovaginal fistula. The entire bladder was involved by tumor at cystoscopy.

CASE III. M.F., a hypertensive, white woman, aged fifty-eight, with a history of "kidney disease" with a clinical Stage IV undifferentiated squamous cell carcinoma of the cervix. The implantation again did not include the bladder floor adequately. Cystoscopy four months after treatment with cobalt showed edema of the bladder floor and trigone area, with marked reduction of the bladder capacity by extrinsic tumor pressure.

The above 3 cases were treated before the smaller needles and adequate bladder floor implantations were designed.

CASE IV. I.V., clinical Stage III, poorly differentiated squamous cell carcinoma of the cervix treated with 5,160 mg. hr. of radium applied to the cervix. Cystoscopy before treatment with cobalt showed the bladder floor to be elevated with bullous edema about the ureteral orifice. There was good renal function with slight hydroureter on the left. Cobalt pattern was designed to omit the previously heavily irradiated area of the cervix. The patient experienced severe and continuous pelvic pain from the time of the cobalt therapy, and two months postoperatively a fistula was noted high on the anterior vaginal wall. In spite of the attempt to prevent central overtreatment there is a possibility that this fistula may have resulted from the superimposition of nearly 7,000 r of cobalt therapy. It is impossible to

confirm this possibility because no placement films of the radium application are available.

Case v. F.P., a woman, aged fifty-four, with a clinical Stage III squamous cell carcinoma of the cervix who had previously received a calculated dose of 2,430 r to the mid-pelvis with external roentgen therapy. At the time of cobalt application seven needles were inserted through the bladder on the *right* side and at the appearance of hematuria, all but one were withdrawn and reinserted at a later date after the remaining needles had completed the planned dosage. The unusual penetration of the bladder was demonstrated roentgenographically to be due to clockwise torsion of the treatment pattern. One month postoperatively a small vesicovaginal fistula developed high in the vagina on the *left* side. It is thought that a significant defect existed in the dosage of the left bladder floor. This was borne out by the fact that the patient has subsequently developed massive tumor involvement of the left pelvis.

Admittedly it is too soon to exclude fistula but with the improvement of pattern across the bladder floor none of the patients who have had implantations done in the past fifteen months have developed fistula. The clinical observations suggest that *failure* to treat adequately in the region of the floor of the bladder is the greatest single predisposing factor in the production of fistula.

2. *Urethra.* Tumor involvement of the urethra indicates such advanced disease that the usual aim is palliation rather than expectation of a cure. Urethral extension of the tumor is usually associated with severe pain. Palliative needle therapy has in our experience led invariably to improved urinary function and a dramatic decrease in the patient's pain. The following case report describes an experience in the management of such an extension by the use of nylon thread cobalt needle technique.

Case vi. M.J. This patient, aged thirty-four, para v, was first seen at University Hospital, eight and a half months pregnant, and with a presumptive diagnosis of cervical carcinoma, clinical Stage II which was confirmed by biopsy as squamous cell carcinoma Grade 3 malignancy. She was immediately delivered by classical cesarean section. External roentgen therapy was given to one anterior and one posterior portal, to a total mid-pelvic dosage of 2,508 r. Upon the completion of external roentgen therapy, interstitial cobalt needles were inserted into the cervical, intermediate and lateral parametrial areas. Within two months after cobalt therapy there was bilateral extension to the pelvic walls, and the Papanicolaou test remained positive for malignant cells.

Four months after cobalt therapy, the patient was readmitted complaining of inability to void and bladder pain. Examination at this time revealed a lemon-sized mass entirely surrounding the urethra. It was evident at this time that the previous dosage pattern had not extended down onto the vaginal cuff. Therefore the entire area of recurrence was included in a new treatment pattern made up of four aluminum needles and twenty-four nylon threads, working both vaginally and through the space of Retzius.

Postoperatively the patient had a gross *E. coli* bladder infection, and the clinical course was characterized by fever, anemia, bladder and vaginal pain. She did, however, regain urinary control for the following two months, at which time the vagina was found to be closed by neoplasm, and she complained of increasing dysuria. A pathologic fracture of the left pubic ramus appeared eleven months after the initial cobalt treatment, and a month later the patient appeared to be in a nearly terminal state.

While the occurrence of pregnancy coincidental with the existence of carcinoma of the uterine cervix makes the eventual outcome almost uniformly certain, this patient did receive limited palliation from the nylon thread cobalt needle therapy. It appears further that if the original treatment pattern had been extended to include the upper half of the vagina, both the patient's prognosis and her comfort might have been somewhat improved.

3. *Ureter.* In 1 patient an interstitial needle penetrated and drained a right hydroureter known from intravenous urograms to exist prior to treatment. Although the patient survived for six months, subsequent fistualization did not occur.

TABLE I

Clinical	Early Group		Intermediate Group		Recent Group	
	Treated	Surviving	Treated	Surviving	Treated	Surviving
Stage I	1	1	1	1	0	0
Stage II	12	2	13	11	6	6
Stage III	10	2	7	7	18	11
Stage IV	2	0	2	2	2	2
Total cases	25	5	23	21	26	19
Rectal reaction	8		7		11	

4. *Bowel.* Penetration by needle is never intentional, and when recognized is withdrawn. Exploratory laparotomy in 12 consecutive cases showed no perforation of bowel on any occasion. There was a rare perforation of the parietal peritoneum but more frequently simply tenting by the blunt needle tip. The needles were found to be in unexpectedly good position as designed. Only small localized hematomas at the base of the broad ligaments were revealed.

A characteristic bowel reaction is recognized in all three stages of development of the study. This development has in general consisted of:

Early group: Treated from August, 1948, to November, 1949. Selected for treatment because of their unfavorable prognosis but offering some remote hope of palliation or cure not thought likely to result from conventional therapy. They were treated with larger diameter needles, fewer total needles, and an uneven pattern with dosages centrally high. They had for the most part been previously treated.

Intermediate group: Treated from January to October, 1950. Characterized by smaller needles, uniform pattern without specific attempt to irradiate the vaginal cuff anteriorly and posteriorly when no tumor seen or palpated in this area.

Recent group: Treated from May, 1950, to March, 1951. Characterized by a more uniform pattern including the vaginal cuff. usually well ahead of visible or palpable tumor extension.

This rectal reaction is biphasic consisting of pain, tenesmus, edema, occasional purulent discharge and bleeding in the first three months followed by low abdominal pain, obstipation, mucus, and occasional bleeding in seven to eleven months. At the later stage the patient may come to colostomy for relief of pain. The patient who weathers this storm will be relatively comfortable subsequently but may die of advancing disease.

There is a very high correlation between the reaction and the position of the needles in relation to the bowel as visualized by preoperative films and gas shadows on the postoperative films. A recent careful review of these cases correlating their implantation films with their subsequent course reveals an adequate explanation for each individual case based upon physical dosage. In general, the lesions in patients with severe bowel reactions have not regressed well. Three explanations have been considered; namely, that they are usually far advanced when first treated, that the infected tumor does not react well to irradiation, or that the systemic defenses against tumor are inhibited. The material available to date is not sufficient for a firm opinion as to the mechanism or mechanisms involved. Two rectovaginal fistulas have been encountered:

CASE VII. B.J., a colored woman, aged twenty-three, clinical classification Stage II, pathological Grade 4 malignancy. The patient had constantly increasing pain and rapidly growing tumor during her postoperative course. Six months after the cobalt implantation she developed rectal bleeding and the rectosigmoid was noted to be fixed in the midline. A month later the tumor had extended to within 3 cm.

of the anal ring. Nine months postoperatively, after severe rectal pain, a rectovaginal fistula developed in the midline. Colostomy relieved some of the pain. The patient died fifteen months after cobalt application with massively widespread neoplasm. It is believed that the cause of this fistula was uncontrolled tumor.

Case viii. M.H., fifty year old treated luetic patient, with squamous cell carcinoma of the cervix which arose twelve years after a subtotal hysterectomy. She had previously had an undetermined amount of roentgen therapy and 2,400 mg. hr. of radium applied to the cervical stump. There was rectal bleeding before she came to our clinic and such severe pain that general anesthesia had to be given to permit the initial pelvic examination. After cobalt needle insertion she became relatively comfortable. Six months after cobalt therapy she developed a rectovaginal fistula at the vaginal apex, 0.5 cm. in diameter. Fourteen months later the fistula persists unchanged and the patient continues to have nearly all her stools per rectum. It is believed that this fistula resulted from heavy retreatment of the central area which had already had 2,400 mg. hr. of radium.

5. *Bleeding.* No severe hemorrhage has been encountered.

Many of the remainder of the cases of carcinoma of the uterine cervix were treated by subpubic plates because of advanced disease for closure of the vagina, for prevention of hemorrhage or possible control of their disease. This has proved an effective and worthwhile method of therapy surprisingly free of complicating features and attended with unexpected freedom from serious pain during treatment.

Others received incomplete treatment for the control of pain, bladder invasion or other complication with accomplishment of the desired effect for the most part.

There were 2 operative deaths, 1 from pulmonary embolism the day after the needles were removed and the other in an advanced case which in retrospect should not have been treated in a definitive fashion because of size of the tumor.

On reviewing these cases in the light of present knowledge, we believe that 6 cases did not profit sufficiently from their therapy to warrant its repetition in similar cases. They had, respectively, a freehand implantation for the control of growth with impending uremia producing death in two months; lucite guided implantation with severe cardiac disease discounted by the medical consultant although there had previously been bilateral pleural effusion, considered noncardiac in origin, and the needles had to be withdrawn before full treatment could be given; the above mentioned patient who had disease involving the peritoneum at autopsy and massive pelvic involvement; 1 case of advanced disease who came for treatment of inguinal nodes; and 1 case with hydroureters advanced beyond hope of salvage. The grading of carcinoma of the uterine cervix by clinical methods was demonstrated to be inadequate to illustrate these complications, especially in the finding of omental and intestinal disease in the group of 12 cases who had routine laparotomies for study of needle placement.

CARCINOMA OF THE VULVA INVADING THE VAGINA

The customary therapy in this clinic is surgical but one opportunity developed to study a case of advanced carcinoma of the vulva unsuitable for surgical management.

Case ix. M.K., a white woman, aged sixty-eight, with a histopathologically proved carcinoma of the vulva which included the entire right labium majus and extended into the right side of the vagina, where it had grossly invaded the bladder base and eroded away the distal half of the urethra. The patient was in constant pain, unable to walk and had complete urinary incontinence. As the lesion was believed inoperable, external roentgen therapy was begun to two perineal portals. After 800 r and 600 r had been administered respectively, the patient's pain became even more intense and it was decided to attempt palliation with cobalt therapy. Nylon threads loaded with cobalt slugs were introduced freehand into the entire tumor area at intervals of approximately 1 cm. and a fairly satisfactory field created. After a dose of 7,000 r had been administered

the threads were removed and the patient voided easily. Now four months postoperatively the patient has gained weight, has neither pain nor bleeding; she is ambulatory and continues to have good urinary control.

CARCINOMA OF THE ABDOMINAL NODES TREATED AT LAPAROTOMY

Two cases have been given what is considered adequate therapy to the pelvic nodes by the insertion of nylon threads into proved tumor. One has gone fourteen months since treatment of a recurrence 4 by 4 by 8 cm. encasing the left iliac vessels and protruding into the pelvis with regression to a mass one-fourth the previous size and no growth for some months. The other had carcinoma of the cervix treated with radium, intravaginal cone therapy and external portals with control of the local lesion but inoperable bilateral iliac and one flat periaortic node mass below the pancreas. These were implanted without untoward result but insufficient time has elapsed to permit evaluation of the therapy. Similar technique in proved but limited metastatic lymph node involvement of the base of the mesentery has given palliation with hope of control, following carcinoma of the colon.

SUMMARY AND CONCLUSIONS

An interim progress report of patients treated with radioactive cobalt by interstitial and contact therapy for carcinoma of the uterus, uterine cervix and vulva with vaginal extension has been presented.

The opportunity for evaluation of the individual problems of tumor extension in relation to dosage administered would in itself justify further study and continuation of the project.

The method provides a freedom of choice hitherto unobtainable and allows better individualization of cases.

Roentgen methods of study of patients with carcinoma of the uterine cervix offers sufficient information to be included as a routine measure and are believed essential to the employment of guided needles. This examination evaluates the extent of diagnosed carcinoma of the cervix and relates this extent to the other pelvic organs.

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DISCUSSION OF PAPERS BY CHAMBERLAIN, KLINGENSMITH AND HALE;* NOLAN, JONES AND NEIL, AND MORTON BARNES, HENDRICKS AND CALLENDINE

DR. HYMER L. FRIEDELL, Cleveland, Ohio. The essayists are to be congratulated for pre-

* The paper by Richard H. Chamberlain, M.D., Paul Klingensmith, M.D., and John Hale, M.S., Philadelphia, Pennsylvania, entitled "Intraperitoneal Injection of Colloidal Radioactive Gold for Advanced Ovarian Carcinoma with Ascites," and read and discussed at the Thirty-third Annual Meeting of the American Radium Society, Atlantic City, N. J., June 7–9, 1951, has not been submitted for publication. It is hoped that the paper may appear in a future issue of the JOURNAL.—ED.

senting a subject which ordinarily engenders a great deal of enthusiasm, with such admirable restraint. I personally feel that radioisotopes will unquestionably add to the armamentarium of radiation therapy. If I had had any of these papers to present, I think I would have been considerably more enthusiastic. I think that the fact that they pointed out the hiatuses that exist in our information and difficulties that may arise with this form of treatment certainly deserves commendation.

My interest for the present moment centers about colloidal gold because of my membership in the Allocation Committee of the Atomic Energy Commission. We have been plagued by some rather trying questions which haven't been completely answered to the satisfaction of all of the members of the committee.

I would like to discuss briefly colloidal gold and tell you how it is used and some of the things that have been bothering us.

Colloidal gold when used intravenously, as you know, will deposit in the reticuloendothelial system because it is a colloid. As a matter of fact, any colloid would do this and it is not because it is gold or because it is radioactive. Chromic phosphate labelled with P^{32}, if converted into colloidal form (really a suspensoid) will do exactly the same thing as will inert colloids. Therefore, if you have reason to irradiate the reticuloendothelial system, colloidal gold is an admirable method of doing it. The radiation, therefore, would occur in the liver, the spleen, and some of the bone marrow, depending somewhat upon the size of the colloid. The size of the colloid will determine how the distribution of the colloids will occur—whether most of it will be in the liver, or most of it will be in the spleen.

Another way that Au^{198} is used, as you heard from Dr. Chamberlain, is to introduce it into cavities. The peritoneal cavity was chosen first by Müller and is a very likely site because metastases are common to the peritoneal cavity, especially from pelvic organs. Ascites, resulting from these metastases, is trying and troublesome and the palliation can be measured by how you control the ascites. The material is deposited about the peritoneal cavity, and if you can achieve reasonably uniform distribution, you can irradiate rather intensively the peritoneal surface. I think that there isn't much question that it is definitely of value.

I have had personal experience with cases that have had ascites in which the ascites appeared to be controlled after treatment with Au^{198}. I must admit however, that the ascites was retarded but without arrest of the tumor masses. Nevertheless, there is real palliation for an interval. As suggested by Dr. Chamberlain, if you get these cases very early, before you have palpable masses, or when the metastases are microscopic, or just after the surgery, it might prove unusually effective.

The third method that gold has been used for is the interstitial administration of this material to irradiate tumors or tumor-bearing areas. Here, I must voice certain reservations. First of all, there are definite problems with regard to uniform distribution. You must remember, as pointed out here, that the average range of the effective radiation, which is primarily beta particles, is something less than a millimeter. Actually, I think it is 0.8 millimeter, which means that you must have very uniform deposition in tissue. Otherwise, you will leave areas which are unirradiated. Or, in order to get enough radiation into the areas which have low radiation levels, you will have to over-irradiate some of the tissue.

In addition to this, you cannot predict, or at least it is difficult to predict, and Dr. Nolan has pointed this out very well, as to whether the colloidal gold will remain in situ. Over the past thirty years we have constantly belabored the fact that we must know something about the radiation dosage and assess it as accurately as possible. When you have difficulty in determining whether material will remain in the tissue, you immediately have great difficulty in deciding what the dosage will be.

I think the important thing with colloidal gold is that colloidal gold, when introduced interstitially, has the property of being taken up by lymph nodes, and here it has a very important advantage over other interstitial radiation because you have an opportunity to irradiate the lymph nodes that are draining the area. Now, if you can be certain that you can get enough drainage from the site of injection so that the lymph nodes are effectively irradiated, then it is possible that this form of treatment could revolutionize the treatment of certain types of cancer. This remains to be seen, as Dr. Nolan has pointed out, and is one of the important situations which must be studied. The prospect that such will prove to be the case, however, is extremely unlikely since there is already evidence to indicate that tumor-bearing lymphatics are generally blocked so

that the gold is transported primarily to the uninvolved lymph nodes.

If you compare radon seeds with colloidal gold, it is clear that for interstitial use they are serving exactly the same purpose. You would, as a matter of fact, avoid some of the problems by using radon seeds in that you can achieve more uniform radiation because you are using long range gamma rays rather than the short range particles. But of course you can never expect radon seeds to be taken up and deposited in the lymph nodes.

One other note of caution. When one uses radioactive gold for interstitial administration, often a considerable amount of pressure is required in the syringe and therefore the equipment has to be as tight as possible. As you know, you can readily protect against a radium or cobalt needle, or a radon seed, and avoid contamination, but colloidal gold is in liquid form and if it escapes in some way, it is obvious that a great deal of annoying contamination will occur. This, of course, is not an insurmountable problem and I am sure that it can be handled very satisfactorily if carefully considered.

In conclusion, I would like to say that the essayists should certainly be encouraged in continuing these studies, and I would like again to congratulate them.

Dr. Alfred I. Sherman, St. Louis, Missouri. The establishment of the use of radioactive colloidal gold as a therapeutic agent in cancer therapy demands many more such excellent experimental investigations such as you have heard this afternoon.

The findings and results which Dr. Chamberlain has presented this afternoon corroborate the findings of Müller in Europe and ourselves in St. Louis, for the use of radioactive colloidal gold as a palliative procedure for malignant ascites due to carcinomatosis peritonei. In the past year and a half we have treated 18 cases of malignant ascites. We have also treated 3 cases with carcinomatosis and palpable masses in the abdomen but without ascites. In 3 cases, radioactive colloidal gold has been injected into the pleural cavity for malignant effusion. These patients with ascites were a selected group. They were all demanding of paracentesis on at least two occasions because of fluid accumulation. They have all had at least one course of roentgen therapy or else have had to discontinue their roentgen therapy because of gastrointestinal complications. We selected this group because it would be easier to evaluate the results over other types of therapy. The results, the dosages, and the method of administration, as a matter of fact, parallel very closely those which Dr. Chamberlain has described.

At the present time we are injecting 100 to 150 millicuries of gold into the ascitic fluid. We drain off as much of the fluid necessary to make the patient comfortable—leaving in as much as possible, so as to act as a method of distributing the gold throughout the peritoneal cavity and to act somewhat as a filter We are giving it in some cases in two applications giving 75 to 100 millicuries (depending on the size of the patient) with each administration—about one week to two weeks apart. Two or three days following the injection of the gold, we withdraw all the fluid, leaving the abdomen flat and the patient comfortable.

Now, to evaluate the results is not too difficult. Some of the patients were terminal and in poor condition and died within three months. To evaluate the results in this group of patients alone, I do not believe fair. However, in all these cases, the patients were made much more comfortable for their remaining days. In many cases, there had been no re-accumulation of fluid, and in some cases, there had been a definite decided decrease in the amount of fluid production. However, in the other group of patients—the group which lived more than three months—there is much more dramatic effect. We found suppression of the fluid for as long as four to eleven months following the treatment. Some cases have been re-treated successfully five and six months later if they developed a recurrence of their fluid.

The results, as Dr. Chamberlain described, are indeed gratifying for no other type of therapy seems to give any better results, and indeed these patients are very uncomfortable untreated. I believe his results and those of others justifies the use of radioactive colloidal gold by this method as a palliative procedure for such cases.

However, the interstitial use of radioactive colloidal gold gives much more promise as an effective type of radiation therapy, not only for carcinoma of the cervix but for other pelvic carcinomas and other anatomically situated lesions, such as the larynx, breast, and the lung. Before it can be entirely evaluated, however, much more work must be done to determine the optimum mode of administration, the dosages necessary to give a cancerocidal effect, the tolerance of various tissues in the body, and the distribution.

The work which Dr. Nolan has presented will be an invaluable aid in attaining these goals. By injecting it under direct visualization he has introduced another interesting approach to the parametrial injection of radioactive colloidal gold. He has also shown that distribution occurs in the various organs of the body and has demonstrated tolerance dosages in the parametria of the monkey.

It is very interesting to note that these tolerance doses are approximately 1.5 millicuries per cubic centimeter of tissue which is almost identical with those which we have found in rabbits and dogs that have been treated. We were very careful, when first using radioactive colloidal gold on humans, not to exceed this dose. However, since then we have found, from recently calculated dosages, that as much as 2 and 2.5 millicuries per cubic centimeter of tissue have been delivered without undue reaction. We believe that this may be somewhat increased, although the upper limits are not yet quite known and must be approached at a very slow and careful rate.

Distribution throughout the organs of the body has been discussed by Dr. Nolan. I believe he uses a 1 per cent pectin solution in which to suspend the colloidal gold. We have found for interstitial use that this will help decidedly in decreasing the entire amount that enters the general circulation.

The oft-repeated question is—Does gold get into lymph nodes which have metastases present? If it does get there, does it get there in enough quantity and does it cure cancer once in nodes? The answer to this question is yet incomplete. However, I think we can say that, from the cases we have treated, there are some who have had metastatic lesions, both in the parametria and in lymph nodes that have shown destruction of tumor.

With the permission of the Society and of Dr. Nolan and Dr. Arneson, I would like to show slides to illustrate some of these changes.

(Slide) Now, this is the method which we use to inject the gold. It is simply an insertion of needles through the vagina into the parametrial tissue and simulates very much that of the insertion of radium needles into the parametrial tissue. The needles are placed in position—two of them laterally, close to the cervix—and two others approximately 2 or 3 centimeters laterally, directed at about a 30 degree angle out in the direction of the anterior superior spine. By the use of rubber tubing a syringe containing the gold is attached to the needles, and as the needles are withdrawn slowly, the gold is injected. We have found that this gives a very effective and safe distribution of the gold throughout the entire pelvis. Only the occasional case has shown spillage to the peritoneal cavity, and this has always been very slight. Measurements which we have done using the scintillation counter, described by Dr. Bonebrake this morning, have shown uniform dosage at selected points in the pelvis. From the gamma-ray measurements, in addition to the beta counts that we have taken on tissue removed at operation, we can get a pretty fair idea of the amount of radiation delivered to various selected points in the pelvis.

(Slide) This shows a lymph node in a patient who had been injected with radioactive gold. You can see that the lymph node itself is entirely destroyed, but there are definite cells still present. This is about five weeks following the injection of the gold and the pathologist will call these definitely metastatic tumor cells but nonviable.

(Slide) This shows other cells which look somewhat like it. It shows the changes which are caused by radiation effects in lymph nodes and on tumor cells.

(Slide) Again, this is a lymph node from a patient who had radioactive colloidal gold injected into the peritoneal cavity. This is six weeks following the injection of the gold. I am showing this slide only to demonstrate the gold particles which are the dark pigmented areas distributed throughout the entire node and the definite radiation effects surrounding it.

It is interesting that although the patient had a great deal of tumor still growing in the peritoneal cavity, none of the lymph nodes, although large and palpable, showed any tumor.

Dr. Gray H. Twombly, New York, New York. I was much interested in these three papers. We have had permission to use colloidal gold in our laboratory for the last six months. In the course of that time, through the cooperation of Dr. Blanchard and Dr. Quimby and the entire staff, we have injected 8 carcinomas of the cervix, and we have treated 3 cases of carcinomatosis of the abdominal cavity.

I would like to ask Dr. Chamberlain first of all about whether he has gone up in his dosage above 100 or 150 millicuries. One of our patients with carcinoma of the ovary received 100 millicuries. This amount has changed the character of the peritoneal fluid from a deep red material, looking much like undiluted blood, to a straw

colored fluid, but has not stopped its reaccumulation, so that a week ago we injected another 100 millicuries into this patient. I would like to ask him whether that is a safe procedure and whether we can go on and give even further therapy with the colloidal gold.

Now, as far as carcinoma of the cervix is concerned, I would like to point out that if this modality of irradiation is merely one of distributing radiation into the areas that can be reached easily by needles, it is certainly not superior to any other method of interstitial irradiation. As a matter of fact, it isn't anywhere near as good as that described by Dr. Morton, because it is not nearly so accurate. The usefulness of this procedure, as I see it, will depend upon whether the radioactive material can get into the lymph nodes in effective concentration or not and how quickly it can do so. If it does not get into the lymph nodes for a month, the radioactivity is gone by that time and you have not accomplished anything.

Now, in the first cases of carcinoma of the cervix that we have attempted to inject according to the technique which has just been described to you, we found the radioactive gold deposited in the pelvis apparently about where the ends of the needles were, and this was very discouraging. Dr. Engel made some observations the other day in another connection, with india ink injected into the cervix. He has pointed out to us a very exciting observation, if it is proved to be so, namely that if one puts colloidal material into the cervix itself, right underneath the mucosa in the canal or into the muscle, that that material gets into the lymphatics almost immediately.

The last case of carcinoma of the cervix which we treated was ten days ago and I operated on this case on Wednesday. We injected 5 millicuries in this patient directly underneath the mucosa into the cervix itself. I am very pleased to report to you that in that operation the lymph nodes draining the cervix were black with the colloidal gold and their counts were very high. As a matter of fact, the counts that we got in the lymph nodes were about one-half the intensity of that found in the cervix itself where the radioactive colloid had been placed.

I wonder whether Dr. Sherman has had any experience with other sites of injection because, in our experience, if you just put colloidal gold into the areolar tissue and the fat of the parametria, you don't get it into the lymph nodes very well.

I would like to make one other comment about Dr. Morton's material. It was been my good fortune to go to Columbus and see his technique and some of his cases. I think that his method of distributing interstitial irradiation is by far the most accurate that I have ever seen. We have here a method of irradiating the pelvis interstitially without producing any hot spots and without producing any cold spots either. They have succeeded in producing a uniform distribution of irradiation through the pelvis. I think this is one of the most interesting and promising methods of irradiation that I have ever had anything to do with or have seen or heard of, because you irradiate the proper areas without irradiating the normal tissues of the skin, of the bones and muscles and so on, surrounding the pelvis.

There is only one criticism that I have to offer of his work. I have already offered it to him in private, so I feel that I can offer it also in public. That is, that if one is interested in the lymph nodes of the pelvis, one is impressed by the fact that these are quite high up—they are way above the place where most radiologists think they are. They run up along the aorta. I think that he and his group have got to devise methods whereby their interstitial irradiation can reach farther up and hit these nodes more accurately than they do at the present time. I would like to have his comment about that.

Dr. James A. Corscaden, New York, New York. Interstitial irradiation is an effort to distribute energy within the object to be treated rather than to reach that object by traversing a lot of normal tissues with the same form of energy, such as we do with external roentgen therapy. The injection of a fluid which would be distributed homogeneously would be the ideal form of radiation, but that fluid has to deliver a certain amount of ionization and do it within a certain time, in order to kill the cancer cells. I am not quite clear as to the amount of actual ionization which occurs in the tissues where colloidal gold is administered by the techniques described. The principle is perfect, if proper ionization is accomplished.

I think that the principle of interstitial irradiation is pretty well established. The idea was presented in 1903. About 1915 it was first really carried out, but I suppose Dr. Waterman is the

only one who has done any great amount of work. The cobalt, in principle, as I see it, is not particularly different from radium. The spectrum is narrower and it may be that there is a more specific effect from the particular wavelengths emitted by the cobalt, but from what advice I can get, so far we have no reason for believing that the cobalt in itself is different from the radium filtered with 0.5 millimeter of platinum.

The device is excellent—if the needles are placed in the right direction. The only questions which I raise are mechanical. It is very difficult to get individual needles into a lesion with much fixation. The placing of the molds—the jigs—offers some difficulties.

The second question is the field of extension of cancer of the cervix. Does it extend in that pyramidal form which we see pictured today in the needles, or is the pyramid's base below, or is it a cylinder? My concept of the pelvis is a sort of a cylinder—that the lymph nodes are lateral to the cervix rather than above it. In our efforts to use needles we have attempted to place the lateral needles parallel to and lying almost in the plane of tissue 0.5 or 1.0 centimeter distant from the obturator fascia. These are just practical questions which come up, but the principle is perfect, and I know that I have seen no pattern of needles applied individually which is as symmetrical and as pretty as these patterns which we have seen in the technique described today.

Dr. Chamberlain (closing). It is very gratifying to have the nice comments from the discussors. I will attempt to answer the question of Dr. Twombly in regard to dosage.

Our dosage in millicuries was arrived at empirically, and in the first group of cases a dosage of 100 to 130 millicuries has seemed to be adequate to suppress fluid formation. The uniformity of distribution of this dose has much to do with its efficacy. I have heard from other sources that similar dosages have failed to prevent reaccumulation of ascitic fluid in some cases. When this happens it is important to know whether the distribution has been uniform, or whether the isotope may have been held into portions of the peritoneal cavity by loculation of fluid. One of our cases has required a second dose of 100 millicuries after an interval of two months.

It seems appropriate to make some comment concerning side reactions and their relationship to dosage. We have noted some nausea and diarrhea with the dosage level of 100 to 130 millicuries. It is sometimes difficult to tell how much of this is due to radiation sickness and how much of it may be due to change in mechanics by the removal of fluid or the disease process itself. I believe that the psychological reaction of the patient to the procedure of having radioactive isotope introduced into the abdominal cavity is a factor of importance. Some of our patients seem to be amused by the idea of having the inside of the abdomen gold-plated. The integral, or whole body, radiation dose is certainly much less with the radioactive gold than it would be for a comparable amount of external roentgen therapy.

Dr. Nolan (closing). I should like to thank the discussants for their comments.

There is one remark I would like to make for Dr. Hare, which was not mentioned in the presentation. Last year, he asked me what happened to the liver—whether the liver was injured. So, blood chemistry studies were done on 14 of these animals two to seventy days after the injection of the gold. The tests included the prothrombin time, the thymol turbidity, and the cephalin flocculation. None of these tests, done before injection and at the time of sacrifice, showed any demonstrable depression of the liver function. However, absolute lymphocyte counts in a very few animals indicated a suppression of the absolute lymphocyte count to about a factor of two; about 4,800 as compared to about 8,000 for a controlled animal living in the same conditions. The control animal counts were similar to those reported for the *Macacus rhesus* monkey.

Dr. Morton (closing). I want to thank the discussants for their extremely kind words.

The lymph nodes known to have had tumor in them have been higher and more posteriorly up about the vessels. We have not seen lymph nodes in the obturator foramen involved after treatment. We are waiting and watching. It is all we can do—to know what the proper shape of applicator might be.

As to the advantages of cobalt over radium, we cannot predict any difference. We like the hard gamma of the cobalt because it permits us to place the implant in the areas adjacent to bone without causing bone necroses. We have seen no radiation bone necroses in about 250 cases treated thus far.

THE EFFECT OF DOSE RATE ON THE LD_{50} OF MICE EXPOSED TO GAMMA RADIATION FROM COBALT 60 SOURCES[1]

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ALTHOUGH the possibility of dependence on dose rate of ionizing radiations has been investigated extensively for such phenomena as mutations, structural changes in chromosomes, mitotic arrest, and lethality in viruses and bacteria,[5] relatively little information seems to be available on time-intensity relationships for toxicity to animals. Boche and Bishop[2] reported an increased lethal effectiveness for rate of a dose of 850 r of 1,000 kv. roentgen rays when delivered in one and one-half minutes in comparison with the same dose delivered in two hours. The data of Casarett[3] on dogs and rats also indicate a decreased effectiveness of roentgen radiation when administered over twenty-four hours rather than when given within five to six hours, although the differences were not marked. Stearner[8] reported that the approximate LD_{50} for young birds was raised about 30 per cent when the dose rate of roentgen radiation was decreased from 43 to 6 r per minute.

In order to contribute information on this question we have estimated, using mice, the LD_{50}'s of gamma radiation delivered at various rates ranging from approximately 5 to 2,500 r per hour.

The results presented here were obtained on mice exposed to gamma radiation from cobalt 60 point and plane sources, with the addition of one datum obtained with a tantalum 182 plane source.[6]

METHODS

The exposures with the point source were carried out in a concrete-walled pit 60 inches long, 24 inches wide, and 42 inches deep. In the floor of this pit was a drain which was 2 feet deep, and which served as a repository for the source when it was not in use. The top of the pit was covered with interlocking lead doors of 6 inch thickness which could be opened with the aid of a travelling overhead hoist. A wooden platform was constructed 20 inches above the floor of the pit to support the exposure cages.

The source for these exposures was a sample of Co^{60} metal, with a strength of 4.5 curies, encased in an aluminum can 2 cm. in diameter and 7 cm. long. This can was placed inside a stainless steel capsule 3 cm. in diameter and 11 cm. long. The upper end of this capsule was fastened to a lead plug of the same diameter into which was screwed a 6 foot length of pipe, by means of which the source could be lifted from the drain into the position where it was used. The upper end of the pipe was fitted so that when the source was elevated, the pipe was attached to a gear reduction motor which rotated the source at a rate of 9 r.p.m. Rotation was found to be necessary, since the aluminum can containing the cobalt had not been centered exactly, and further manipulation was considered unsafe.

The exposures were carried out in two semicircular cages constructed of perforated aluminum mounted on plywood sheets. When in position, they formed a circular cage with a center opening of 4 cm. diameter for the source. The cages were composed of six concentric circles, each circular row being segmented into cubicles large enough for one mouse. For exposure the mice were placed into the cubicles of a particular row, and the cages placed on the shelf in the pit; the point source was then raised

[1] The work described in this paper was conducted under a research contract supported by the Atomic Energy Commission and administered through the Medical Division, Chemical Corps, United States Army.

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so that the Co^{60} was at the level of the cage.

Calibration was carried out by the use of Victoreen r-meters, placed in the center of each cubicle. The average deviation of the dose among the compartments of a given row was less than the average deviation of separate readings in a given cubicle.

Carworth CF-1 female mice were used in all of these experiments. Most of them were two to three months old, weighing an average of 25 gm. All mice were coded by ear punch prior to exposure, so that any major irregularities in dose among the different compartments would have been detectable.

The details of the construction of the Co^{60} plane sources are described elsewhere.[9]

Mortalities were based on a thirty day observation period. Although most of the animals were observed for longer periods of time, only one death was observed in an additional thirty day observation period among some 300 mice living more than thirty days after exposure.

OBSERVATIONS

The effect of the dose rate on the LD_{50} of gamma radiation for mice is shown in Table 1, which includes, in addition to four point source determinations, three plane source measurements, two with cobalt 60 and another with tantalum 182. The method of Litchfield and Wilcoxon[7] was first used to calculate the LD_{50}'s and their limits; subsequent calculations by the method of Bliss[1] gave virtually the same results.

The equations for the regression lines, wherein Y is the mortality in probits and X is the $\log_{10}$ of the dose, as calculated by the method of Bliss,[1] are also included in Table 1. Chi-square estimations indicated that none of the probit-log dose plots deviated significantly from linearity.

It is evident that although the LD_{50} was approximately constant for dose rates from 240 to 2,530 r/hour, it rose sharply as the rate was decreased below 240 r/hour. This increase in the lethal dose was accompanied by a marked decrease in the slope of this probit-log dose curve.

For the maximum rate used, 2,530 r/hour, the LD_{50} was 772 r; for 250 kv. roentgen radiation delivered at approximately the same rate (2,800–3,000 r/hour) the LD_{50} as determined in this laboratory[4] for the same strain and sex of mice was 560 r.

TABLE I

LD_{50} ESTIMATIONS IN MICE EXPOSED AT DIFFERENT DOSE RATES TO GAMMA RADIATION

Dose rate (r/hr.)	Regression Line[1]	Hours for LD_{50}	No. Mice	LD_{50} (r) with Limits (p=0.05)	Source
2,530	5.183+17.801 (X-2.896)	0.305	254	772 (754–791)	Point Co^{60}
896	4.826+16.882 (X-2.896)	0.88	80	785 (738–814)	Point Co^{60}
240	5.236+14.273 (X-2.917)	3.33	140	800 (760–841)	Point Co^{60}
87	4.426+12.292 (X-2.958)	11.6	120	1,010 (956–1084)	Point Co^{60}
37	5.022+ 6.265 (X-3.079)	31.9	96	1,081 (985–1415)	Plane Ta^{182}
6	5.227+ 3.385 (X-3.287)	276	100	1,658 (1352–2020)	Plane Co^{60}
4.8	—	576*	60	2,760	Plane Co^{60}

* Estimated from two exposure times.

[1] Bliss. See references.

DISCUSSION

The dependence of the LD_{50} for mice on the rate at which gamma radiation is administered can be explained on the basis of accommodation by the animal to the effects of radiation provided the dose rate is sufficiently low. This accommodation, or "recovery," became significant in these experiments when the dose rate was lowered from 240 r/hr. to 67 r/hr.

It should be possible to quantitate this effect of dose rate. A first approximation has been made using the formula employed by Lea[6] for the effects of intensity on reduction of mitotic activity:

$$D_0 = I\tau(1 - e^{-t/\tau})$$

which can be rearranged to:

$$It = D_0 \frac{(t/\tau)}{(1 - e^{-t/\tau})}$$

where I is the intensity (in roentgens per hour, in this case) t is the exposure time (in hours) required to produce 50 per cent deaths, D_0 is the effective dose (r) required to produce 50 per cent deaths, and τ is the half-accommodation, or half-recovery, time in hours.

Inspection of the data shows that the effective LD_{50}, D_0, would probably be in the vicinity of the observed LD_{50} for the highest dose rate used, in view of the relative independence of the LD_{50} on the dose rate in the range of 240 to 2,530 r/hr. Assuming a value of 770 r for D_0, we found that for τ a value of twenty-five hours provided a curve which accounted satsfactorily for the data obtained at dose rates ranging from 2,530 to 37 r, the predicted curve (Fig. 1) passing within the fiducial limits ($p=0.05$) for the estimated LD_{50}'s.

However, these constants do not account for the data obtained at dose rates of 6 r/hr. and below. It is almost certain that the phenomenon of recovery of animals from radiation injury is too complex to be accounted for in terms of a single recovery constant, and that at least a second constant, of approximately ten times the order of magnitude of the first, but of relatively little importance for short time intervals, will have to be incorporated into the formulation in order to account for all of the data.

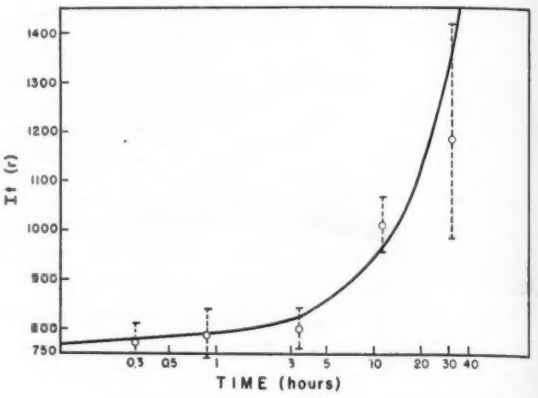

FIG. 1. Variation in LD_{50} (It) as a function of exposure time. The curve was calculated from the equation in the text. The points were determined experimentally; the vertical projections from each point represent the fiducial limits for $p=0.05$.

SUMMARY

The LD_{50} for mice exposed to gamma radiation is relatively independent of dose rate between 240 and 2,530 r per hour. At lower dose rates, the LD_{50} was appreciably higher. Between 37 and 2,530 r per hour, the variations can be accounted for in terms of a single recovery constant.

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STUDIES ON THE EFFECTS OF CONTINUOUS EXPOSURE OF ANIMALS TO GAMMA RADIATION FROM COBALT 60 PLANE SOURCES[1]

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NUMEROUS studies on the effects of repeated sublethal exposures to gamma and roentgen radiation on the survival of animals have been carried out, most of which have consisted of daily exposures of animals to roentgen-ray doses given in high intensity over short periods of time. The experiments of Sacher[8] and of Hagen and Simmons[3] are examples of this type. Lorenz *et al.*[4,5] studied the effect of gamma radiation from a radium source on survival of animals exposed eight hours per day to daily doses of 0.11 to 8.8 r per day. Except for some roentgen therapy studies such as those summarized by Medinger and Craver,[6] few experiments have been carried out in which animals were exposed continuously, twenty-four hours per day, for varying periods of time or until death occurred.

The experiments presented here are concerned with the survival of rats, mice, and guinea pigs exposed continuously to doses of external gamma radiation ranging from 15 to 140 r/day. Some experiments were also carried out with limited exposures of the animals.

METHODS

Exposure Chambers. Irradiation was carried out from plane sources, consisting of solutions of cobalt 60 chloride contained in sealed trays, 30 by 30 inches in surface area and ½ inch deep, constructed of 0.6 mm. stainless steel. These capsules were supported in welded angle-iron frames, around and over which was placed a 4 inch thickness of interlocking lead bricks. The first chamber was constructed so that the animal cage was attached to the chamber door; closing the door caused the cage to be centered over the source. The radiation dose could be varied by a factor of approximately eight by altering the distance between the source and the floor of the cage. The second chamber was fitted with two capsules, so that three cages of animals could be used: one above, one below, and one between the capsules. The dose was relatively inflexible in this chamber, and could not be altered to a large extent except by changing the concentration of emitter within the capsule or by interposing shields between the source and the animals.

The cages used with the first chamber were made of 0.6 mm. stainless steel, and were 24 by 24 inches in cross section and 12 inches deep. The removable cage floor was made of perforated aluminum reinforced with hardware cloth. The cages designed for the second chamber were 20 by 20 by 5 inches. These were constructed of hardware cloth and supported on galvanized iron trays.

Calibration. The dose delivered was estimated on the basis of numerous measurements made by means of Victoreen condenser r-meters, placed at a distance from the cage floor equal to the half-thickness of the animal under study. Since the area of the source was not infinitely larger than the area of the cage floor, the dose measured in the corners and along the sides of the cages was about 5 per cent lower than the values observed in the center of the cage. This difference was partially eliminated by blocking

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off the corners with receptacles for food and water. All dose rates cited were based on averages of at least ten separate measurements in different areas of the cages. The average deviations of the average measurements were about ±3 per cent.

Attempts to use film badges implanted subcutaneously in rats showed poor reproducibility from one experiment to another, probably attributable to slight variations in the processing of the film at different times. Within a given experiment, however, the degree of exposure of films in different animals of the same group was excellent, indicating a homogeneous exposure of these animals.

Animals. Female rats, mice, and guinea pigs were used throughout. The rats were Sprague-Dawley albinos. Except for those used in a few experiments, they were three to four months old and weighed between 190 and 240 gm. when introduced into the chamber. The guinea pigs were hybrids obtained from the Department of Zoology of the University of Chicago. They were eight to ten weeks old when used, and weighed between 250 and 400 gm. The mice were of the Carworth CF-1 strain, six to ten weeks old, weighing between 20 and 28 gm.

Mice and rats were fed Wayne Dog Blox and water *ad libitum* as a standard diet. Guinea pigs received Purina rabbit pellets and water, supplemented by fresh cabbage three times a week.

The temperature of the room in which the chambers were situated was maintained at 74° F. Control animals were also housed in this room.

The exposed animals were given fresh food and water daily, and were transferred to clean, sterilized cages as often as necessary, usually every day, depending upon the number of animals involved. The animals in the chambers were weighed at least once a week. Except when removed from the chambers for the purposes of weighing and cage changing (seldom requiring more than ten minutes), the animals were continuously exposed to gamma radiation.

Since the primary purpose of these experiments was to study toxicity, it was felt that excessive manipulation of the animals was to be avoided. Hence, no hematologic studies were carried out. A few obviously moribund animals were sacrificed for histopathologic

TABLE I

EFFECT OF VARIATION OF DOSE RATE ON THE SURVIVAL OF RATS EXPOSED CONTINUOUSLY TO GAMMA RADIATION FROM A COBALT 60 SOURCE

Dose rate (r/day)	No. Rats	Death Times (days)			Mean Survival Time (days)	σ	Mean Accumulated Dose (r)
		First	Median	Last			
120	20	22	39	51	39.0	5.8	
	20	19	39	54	36.6	8.3	
Total:	40	19	39	54	37.8	7.2	4,540
90	20	17	52	62	45.5	13.1	
	20	38	53	67	51.3	10.1	
Total:	40	17	52	67	48.4	11.2	4,350
80	20	35	55	82	53.3	11.8	
	20	38	52	75	52.7	8.0	
Total:	40	35	54	82	53.0	10.1	4,240
70	20	34	68	116	72.4	20.8	5,070
60	25	135	225	370	236.0	53.6	14,160
20	17	165	361	443	332.6	95.8	6,652

TABLE II

EFFECT OF VARIATION OF DOSE RATE ON THE SURVIVAL OF MICE EXPOSED CONTINUOUSLY TO GAMMA RADIATION FROM A COBALT 60 SOURCE

Dose rate (r/day)	No. Mice	Death Times (days)			Mean Survival Time (days)	σ	Mean Accumulated Dose (r)
		First	Median	Last			
140	20	7	19	22	22.0	9.6	3,080
115	18	19	35	61	36.8	10.5	4,230
90	100	14	53	112	51.6	23.6	4,640

examination, and in one experiment 2 apparently healthy mice were removed from the chamber for microscopic study of their tissues. Otherwise, only gross pathologic examination was made. A number of dead animals, particularly rats, were so extensively eaten that no postmortem examination was possible.

RESULTS

Mortality. The effect on the survival of rats of continuous exposure to gamma radiation at varying dose rates is shown in Table I. It can be seen that, at dose rates of 80, 90, and 120 r per day, the mean accumulated dose was approximately constant. There was a slight increase at 70 r/day and an appreciable increase at 60 r/day in the average amount of total radiation accumulated by the rats. Although the rats exposed to 20 r/day outlived the 60 r/day group by over 100 days, they accumulated only slightly more than half as much radiation.

Three groups of mice were exposed to doses of 90, 115, and 140 r/day. The survival data are presented in Table II. There was a negligible difference between the mean accumulated doses of the 90 and the 115 r/day groups; however, the average dose accumulated by the mice exposed to 140 r/day was significantly reduced.

Survival figures for guinea pigs are shown in Table III. In contrast to the observations on rats, the mean accumulated dose was relatively constant for dose rates ranging from 20 to 120 r/day. The apparent maximum occurring at 60 r/day cannot be considered significant.*

Limited Exposures. For a few of the dose rates studied, animals were exposed for varying lengths of time and then removed and observed for late deaths. Several groups of 10 guinea pigs each were exposed to 90 and to 120 r/day for time intervals ranging from five to thirty days. From the mortality data based on deaths occurring within the thirty day peri-

* It is perhaps of some interest to point out that the experiment carried out with rats exposed to 60 r/day also gave results which were slightly out of line. These experiments were carried out consecutively in the same exposure chamber; and while we feel that the estimation of the dose was accurate to within at least 6 per cent, it is conceivable that some unrecognized environment factor was favorably influencing survival in these two experiments.

TABLE III

EFFECT OF VARIATION OF DOSE RATE ON THE SURVIVAL OF GUINEA PIGS EXPOSED CONTINUOUSLY TO GAMMA RADIATION FROM A COBALT 60 SOURCE

Dose rate (r/day)	No. Guinea Pigs	Death Times (days)			Mean Survival Time (days)	σ	Mean Accumulated Dose (r)
		First	Median	Last			
120	20	11	17	29	18.4	5.7	2,210
90	20	14	19	28	20.2	3.8	1,820
60	20	32	41	53	41.3	5.6	2,480
30	20	22	60	102	62.8	17.3	1,880
15	20	53	98	207	105.6	34.5	1,580

TABLE IV

SURVIVAL AND INCIDENCE OF TUMORS IN RATS EXPOSED TO 120 r/DAY FOR 10 AND 20 DAYS

	1,200 r 10 Day Exposure		2,400 r 20 Day Exposure		Additional Controls	Total, All Controls
	Control	Exposed	Control	Exposed		
No. rats	7	20	9	20	12	28
Acute deaths*	—	3	—	6	—	—
No. surviving	7	17	9	14	12	28
First death (day)	290	159	222	105	349	
Median death	471	361	448	315	487	
Last death	553	483	664	467	651	
Average survival (days)	432	364	413	316	494	
Approximate age at end of exposure (days)	160	160	140	140	100	
Total life span (days)	592	524	553	456	594	585
Decrease due to exposure (days)	—	68	—	114	—	—
Rats with tumors	3	14	3	11	4	10
Average time of appearance of tumors (days)	246	251	390	252	518	404
Total number of tumors	4	22	4	18	8	16

* Within 30 days after removal from exposure chamber.

od after termination of exposure, the LD_{50} was calculated for the two dose rates by the method of Bliss.[1] For guinea pigs exposed to a dose rate of 90 r/day, the LD_{50} was estimated to be 950 r, and for 120 r/day it was 900 r. This difference is not a significant one, although it shows a tendency for the LD_{50} to decrease with increasing dose rates, a fact established with mice acutely exposed to Co^{60} gamma radiation at dose rates varying from 2,500 to 87 r/hour,[9] and confirmed at lower dose rates: the LD_{50} for mice exposed to 140 r/day was 1,658 r, while for mice exposed to 115 r/day the LD_{50} was estimated to be 2,760 r.

Three groups of 20 rats each were exposed to 120 r/day for ten, twenty, and thirty days. All of the animals exposed for thirty days died, the mortality curve almost exactly paralleling that seen in rats exposed to 120 r/day until death. Three rats died during the thirty day observation period following a ten day exposure, and after a twenty day exposure the mortality was 6/20. The LD_{50} for this group would thus seem to be somewhere between 2,400 and 3,600 r. The survivors of these experiments, 17 rats which had received 1,200 r and 14 rats which had received 2,400 r, were kept for their lifetimes, along with groups of control rats of the same age as those exposed. It was observed that both groups of irradiated animals had a shorter life span than their controls, and that the groups exposed for ten days outlived those exposed for twenty days (Table IV).

Incidence of Tumors in Rats. There was a significant increase in frequency of subcutaneous tumors among the survivors of the groups of rats exposed for ten and twenty days to 120 r/day (referred to in the preceding paragraph), in comparison with their controls (Table IV). Of the 17 rats surviving the immediate lethal effects of a ten day exposure (1,200 r), 14 died with tumors; 5 of these animals had multiple tumors. Tumors had been seen in 9 of the 17 rats within 280 days after termination of exposure. Similar data were recorded for the group exposed for twenty days (2,400 r): 11 of the 14 rats died with tumors, 5 rats had multiple tumors, and half of the animals developed tumors within 290 days after removal from the exposure chamber. In contrast, among a total of 28 control rats observed throughout their lifetimes, only 10 died with tumors; at a

time when half of the exposed animals had developed tumors only 1 could be detected among the controls.

Two of the rats exposed continuously to 60 r/day developed tumors. These were noted after 126 and 265 days of exposure. Of the 17 rats continuously exposed to 20 r/day, 11 developed tumors, these appearing between 115 and 381 days of exposure, with a median of 269 days.

In an experiment not yet completed, 40 rats were exposed to 100 r/day for fourteen days. Two of these animals died within a short time after termination of exposure, and these deaths were attributed to a direct effect of irradiation. Eleven of the 38 survivors died without tumors: tumors developed in all of the others, of which only 1 rat is still living (588 days after removal from the chamber). Eight tumors have been noted after 588 days of observation of a group of 20 control animals; 4 of the controls are still living. The difference in median survival time between the control and exposed groups was fifty-eight days.

We did not observe any tumors in our guinea pigs or mice, none of the experiments with these species having lasted more than 207 days.

Weight Changes. The body weights of irradiated guinea pigs generally increased at the same rate as or, in some cases, at a slightly greater rate than in the controls, regardless of the dose employed. In a number of animals the body weight dropped sharply in the week or two preceding death, but this was not an invariable finding.

In mice and, more particularly in rats, however, there was an initial weight loss, the extent of which seemed to vary with the degree of irradiation, after which there was a limited period of weight gain. After this phase of relative stabilization of weight, there was a second, often precipitous fall in body weight of most animals. For example, the rats exposed to 60 r/day lost, on the average, 55 gm. in the four weeks prior to death, 25 gm. in the last week alone. Only 1 rat which died shortly after ulceration of a tumor failed to show this pre-mortal weight loss.

Various modifications were made in the experimental conditions, such as alteration of the diet, illumination of the chamber, and reduction of the number of rats exposed, in order to try to detect an environmental factor other than irradiation which might be contributing to the initial weight loss in rats. Addition of canned raw meat to the diet seemed to lessen somewhat the initial decrease in weight, but failed to influence survival. Illuminating the chamber fifteen hours per day failed to influence weight loss, and reduction of the number of rats exposed from 20 to 5 also did not alter the decrease, an indication that possible overcrowding and diminished access to food and water were not important factors in our experiments.

A significant correlation between survival and either the pre-irradiation weight or the rate of initial decrease could not be established.

*Pathologic Changes.** Atrophy of the spleen, thymus, bone marrow, and ovaries were consistent findings in all exposed animals which had been sacrificed when moribund. Jejunitis was commonly observed in rats and mice exposed to the higher dose rates, and the effects on the intestine seemed to be strongly suggestive as the principal single cause of death in these animals. At lower dose rates, 20 and 60 r/day, anemia with subsequent anoxia was the most probable factor in many rats, since terminal convulsions were often noted, but lack of hematologic data makes this supposition impossible to confirm. In some of the rats exposed to 20 r/day, death was attributed to sepsis following ulceration of a subcutaneous tumor.

In guinea pigs, intestinal hemorrhage was by far the most pronounced gross observation. Epilation was occasionally seen, and subcutaneous hemorrhages were often observed.

Among the control animals, as well as those exposed for limited times, pulmonary changes were most pronounced at autopsy, although death following ulceration of subcutaneous tumors was fairly common. Internal tumors were not discovered in any of the animals autopsied.

DISCUSSION

It is of interest to compare the survival of rats and mice continuously exposed to gamma radiation from Co^{60} with the survival of those exposed to daily doses of roentgen radiation. The survival times of rats and mice plotted as a function of the daily dose are shown in Figures 1 and 2,

* We are indebted to Dr. John B. Storer for much of the autopsy data.

respectively, along with the data of Hagen and Simmons[3] and Sacher.[8] The parallelism is quite close in the case of the two rat curves, a factor of approximately two separating the daily dose required for the same death times. Our data on the survival of mice are not as extensive, but it appears, at least within the limits of the dose ranges studied, that for mice as well as rats continuous gamma radiation is about one-half as effective as repeated roentgen irradiation.

Part of this discrepancy is due to the difference in specific ionizations of 250 kv. roentgen radiation and 1.1–1.3 mev. Co^{60} gamma radiation. For CF-1 female mice, the LD_{50} for gamma radiation, 772 r (ref. 9) is about 1.4 times that for roentgen radiation, 550 r (ref. 2), given at similar dose rates.

It has been further shown that the acute LD_{50} for mice is about 1.4 times greater when the dose of gamma radiation is administered in a twenty-four hour period than when it is given in 0.3 to three hours.[9] Thus the two-fold difference between the

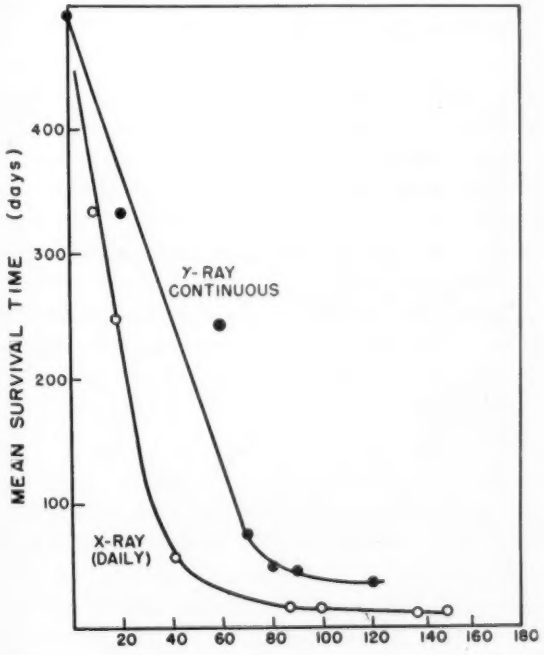

Fig. 1. Survival times of rats exposed to varying daily doses of gamma or roentgen radiation. The roentgen-ray data were obtained from Hagen and Simmons.[3]

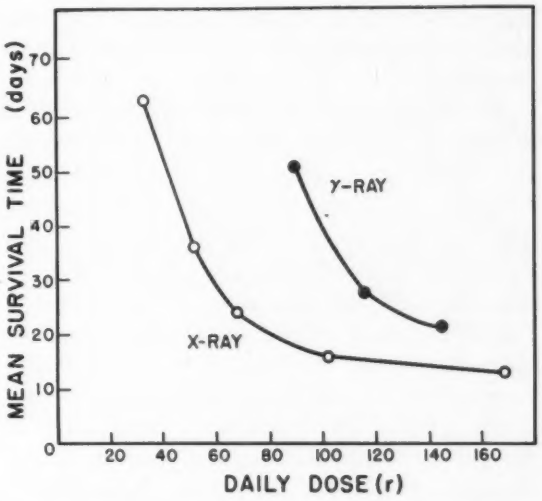

Fig. 2. Survival times of mice exposed to varying daily doses of gamma or roentgen radiation. The roentgen-ray data were obtained from Sacher.[8]

daily dose of continuous gamma irradiation and repeated roentgen irradiation required to effect the same mean death times can be accounted for in terms of two empirically derived factors, of approximately equal magnitude, one relating to specific ionization and the other to time-intensity.

An attempt to relate continuous gamma radiation toxicity to acute roentgen-ray or gamma-ray toxicity must take into consideration the phenomenon of recovery. A simple formulation of the recovery factor has been discussed in some detail by Hagen and Simmons.[3] On the basis of their experiments with divided doses of roentgen radiation, they found that their data could be related best by the expression:

$$R_t = D(1 + r)^t \tag{1}$$

where R_t is the "effective" dose remaining at a time t after administration of a single measured dose D, and r is the recovery rate per unit time (r is a negative number.)

For continuous or repeated exposure, the expression becomes:

$$R = \frac{D}{r}[(1 + r)^t - 1] \tag{2}$$

where D is the measured dose rate in r/day, t is the number of days exposed, and r is

the exponential recovery rate, as a fraction of the cumulative dose recovered from per day.

As Hagen and Simmons point out, this concept has severe limitations. First of all, according to the equation there will be a maximum value for the effective dose R, equal to $-D/r$ (r being a negative number); and if this maximum effective dose is less than the lethal dose, the animal would never die as a result of irradiation. Further, it is most probable that the recovery rate is not constant, but like many homeostatic mechanisms will vary with the intensity of the stimulus and the resultant damage produced. However, it is of interest to test this equation to see whether a single factor can account for some of the differences between acute radiation mortality data on the one hand, and chronic experiments in which there is relatively slight variation in experimental conditions on the other hand, so that a single empirical factor of recovery might conceivably apply.

The method used by Hagen and Simmons to calculate a recovery rate in rats consisted of giving a fraction of an LD_{50} dose to a group of rats, and then at various time intervals thereafter measuring how much additional radiation was required to produce death. The difference between the actual value of the total dose administered and the single dose LD_{50} was taken as a measure of the amount of the initial dose from which the animal had recovered. From these data, a recovery rate of -0.082 (8.2 per cent per day) was calculated.

We have estimated recovery rates for guinea pigs and mice by a different procedure. If LD_{50} measurements are made at two slightly different dose rates of low intensity, it can be assumed that factors of time *vs.* intensity will not be important, and that the "effective" LD_{50} dose, R, will be the same in both experiments. The difference between the observed LD_{50} doses can then be attributed to a longer time for recovery at the lower dose rate. From the data on LD_{50} measurements on guinea pigs mentioned previously (10.6 days at 90 r/day = 954 r; 7.5 days at 120 r/day = 900 r), a recovery rate of -0.039, or 3.9 per cent per day, was calculated. This value cannot be regarded as much more than an indication of an order of magnitude, since only 50 animals were used in each LD_{50} determination.

On the basis of this value for recovery rate, an "effective" LD_{50} was computed, and was found to be 780 r, or about two to three times the range of values (225–400 r) reported for the acute roentgen-ray LD_{50} dose.[2]

A similar type of calculation was carried out for mice, with a resultant value of -0.114 per day as the recovery rate. The "effective" LD_{50} for dose rates of 140 and 115 r/day was calculated to be 990 r, or about 1.8 times the acute roentgen-ray LD_{50}.[2] The order of magnitude of this recovery rate of 11.4 per cent per day was confirmed in another manner: groups of mice were pre-treated with doses of gamma radiation varying from 100 to 400 r at a rate of 32 r/minute, and were then exposed until death at a rate of 115 r/day. It could be shown that the biological effectiveness of the low dose rate, 115 r/day, delivered over a period of twenty-four days, was equal to 31.8 r/day of gamma radiation delivered at a rate of 32 r/minute, and that this difference in effectiveness implied a recovery rate of about 10 per cent per day.

We have not used the LD_{50} method to estimate recovery rates in rats. However, application of the value of 8.2 per cent per day obtained by Hagen and Simmons to the estimated LD_{50} for rats exposed to 120 r/day (assuming the value to be 3,000 r) gives an "effective" LD_{50} of 1,310, or about 2.2 times the acute roentgen-ray LD_{50},[3] a factor of the same order of magnitude as seen with mice and guinea pigs.

Thus in all three species tested, recovery rates can be calculated, which, when used to compute effective doses administered at dose rates of the order of 100 r/day, will yield values which are approximately two

to three times the LD_{50} for acute roentgen irradiation.

Then when such factors as specific ionization and time-intensity are considered as mentioned previously, the additional factor of two can be accounted for after correction for recovery rates, and a close empirical relation can be established, at least under a fixed set of experimental conditions of relatively narrow variation, between high intensity roentgen-ray and low intensity gamma-ray toxicity.

An additional method of calculating recovery rates is suggested by the data on the effect of limited exposures on longevity. It has been shown that a single dose of roentgen radiation will shorten the life span of a female rat by approximately 0.22 day/r administered.[9] In the experiment summarized in Table IV, an exposure of 1,200 r (120 r/day for 10 days) from a gamma source decreased the average survival of rats by sixty-eight days, while 2,400 r produced a decrease of ninety-seven days. In terms of roentgen radiation, 1,200 r from a Co^{60} source would be equivalent to 310 r, and 2,400 r to 440. The original data are too limited to enable one to place much reliance on this method of calculation, although it is of interest to note that the estimated recovery rate was calculated from these data to be -0.083, in close comparison to the value of -0.082 established by Hagen and Simmons. The calculated "effective" gamma-ray doses required to produce the aforementioned decreases in life span are 2.7 times the roentgen-ray doses.

In order to extend these calculations to lower dose rates used in the studies on rats and guinea pigs, more information would be required, particularly concerning the LD_{50} dose, as distinguished from the mean survival time. Without these data, certain assumptions must be made concerning the intervals between the time at which the animal died during exposure and the time at which it had accumulated enough to produce death without further exposure. These assumptions are so uncertain that almost any empirical treatment might be fitted to the data. It is obvious that the recovery phenomenon is too complex to be expressed in a single term; such factors as the degree of irreparable damage, the effect of dose rate on recovery rate, and the variation in recovery rate with the age of the animal will have to be considered in an attempt to relate rat mortality data at dose rates of 20 r/day to acute toxicity data.

SUMMARY

The effect on survival of rats, mice, and guinea pigs exposed to continuous gamma radiation from a cobalt 60 source at dose rates ranging from 15 to 140 r per day have been observed. Both duration of life and limited exposures have been carried out, and median lethal doses have been calculated for several dose rates. Under slight variations in experimental conditions, low intensity gamma-ray exposure data can be related to acute roentgen-ray or gamma-ray toxicity data through certain empirical factors for time-intensity (1.4), specific ionization (1.4), and recovery (4 to 11 per cent per day).

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NITROGEN BALANCE IN MALIGNANT DISEASE

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LEADING the immediate causes of death from cancer are those causes directly related to cachexia.[45] Cachexia is the slow wasting process which enfeebles the individual, reduces his resistance to infection, and slows down metabolism. The effect of cachexia on survival is not known, nor has the mechanism giving rise to cachexia been satisfactorily explained.[3,31,33,42]

In view of the wasting of protein-bearing tissues, it is assumed that cachexia is associated with negative nitrogen balance; that is, a greater excretion of nitrogen through the urine and feces than is taken in orally or parenterally.

Malignant disease, even localized, is usually associated with hypoproteinemia, particularly depression of the plasma albumin fraction.[5,7,11,27,35] Due to the dehydrating effect of chronic disease, hypoproteinemia may not become apparent until normal hydration is restored.[1,40] Apparently hypoproteinemia is a manifestation of the general protein withdrawal from all body tissues. It has been found that the relationship of plasma albumin to total body protein is maintained in health and disease at a ratio of 1 to 30.[41,46]

In nonmalignant disease, negative nitrogen balance can readily be reversed by high nitrogen intake, either orally or parenterally.[13,19] If cachexia could be reversed in malignant disease, the prevention of its pernicious effects might be possible, and tolerance to roentgen therapy, often limited by a poor nutritional state, might be increased.

This paper deals with an investigation of the magnitude of nitrogen loss in malignant disease, the influence of roentgen therapy on nitrogen balance and the effects of various diets on protein synthesis, with particular attention to the effects of a high protein intake on the nitrogen balance of the cachectic individual.

Normally, the avenues of nitrogen loss are the urinary and gastrointestinal tracts, with an insignificant loss through perspiration. The urinary nitrogen is a product of endogenous metabolism and the spill of excess protein not required for maintenance and growth. Fecal nitrogen is relatively constant in a given individual in the absence of diarrhea or other gastrointestinal disease causing impaired absorption, and represents the protein content of fecal bacteria.[6]

Urinary nitrogen values are increased with fever, acute and chronic disease, immobilization and physical insult whether in the form of fracture, crushing injury, or radiation therapy.[14,24,33] Abnormal avenues of nitrogen loss develop as a result of wounds, burns, infections with hemorrhage or exudate, effusions, edema, or ascites. Under these circumstances, nitrogen loss tends to overcome a normal nitrogen intake.

EFFECTS OF NEGATIVE NITROGEN BALANCE

Whatever the cause of negative nitrogen balance, the effects are similar and multiple. A drop occurs in the level of hemoglobin and plasma proteins and in muscle and organ volume. Numerous investigators believe that these forms of protein are in a dynamic equilibrium.[38] The production of erythrocytes, leukocytes, hormones and enzymes is impaired by persistent nitrogen loss. A drop in certain globulin fractions reduces antibody production.[9] Rhoads[36] has demonstrated the development of hepatic dysfunction in hypoproteinemia.

Clinically, the symptoms of hypoproteinemia manifest themselves as anemia, disuse atrophy, weakness and susceptibility to infection. Impaired wound healing, decubitus ulcers, and edema of the gastrointestinal mucosa with paralytic ileus and impaired absorption may also occur.[4,19,26,32]

Acute nitrogen loss occurs after severe trauma or acute illness, and is intense and

self limited. Chronic nitrogen deficit is associated with chronic or recurrent disease. In a series of patients with chronic nitrogen deficit and non-neoplastic disease, Browne, Schenker and Stevenson[8] were able to produce nitrogen retention by high nitrogen diet at an earlier date and at a lower level of protein intake than in cases with acute nitrogen deficit. At the time of writing, I could find no report of attempts at altering chronic negative nitrogen balance in patients with malignant disease.

NITROGEN BALANCE IN HEALTH

The nitrogen requirements of the healthy active individual have been studied by Chittenden.[10] He found that the minimum daily intake for maintenance was fairly uniform and varied from 0.10 to 0.12 gram per kilogram of body weight. A man of average size, weighing 70 kilograms, would therefore require 7.0 to 8.4 grams of nitrogen daily. As 1 gram of nitrogen is present in 6.25 grams of protein, nitrogen balance would be maintained by 44 to 53 grams of protein when accompanied by adequate fats and carbohydrates to satisfy energy needs. All proteins must be of high nutritive value; that is, contain all of the eleven essential amino acids in copious quantities. The remainder of the amino acids can be synthesized by man.[39]

The Sherman diets for civilian hospitals are based on the needs of healthy individuals and will deliver protein in excess of minimum requirements.[43] The regular hospital diet contains 11.2 grams of nitrogen and will supply the average individual with 1 gram of protein per kilogram of body weight daily. The high protein diet contains 19.2 grams of nitrogen.

PROTEIN HYDROLYSATES

In acute or chronic disease, the nitrogen requirements are multiplied over that in health, so that even the high nitrogen diet may be inadequate. The diet is easily supplemented by skim milk powder or casein digests, which are the most compact sources of readily utilized protein. Up to 700 grams of protein can be taken in twenty-four hours in this manner—the equivalent of 6 pounds of beefsteak.[6]

Elman[20] found that patients assimilated casein digests when they were unable to retain the nitrogen of whole protein. The enteric canal is the most efficient route for absorption, whether the route of delivery is oral or via gavage or gastric drip. However, refined casein digests may be given intravenously with carbohydrate and vitamins sufficient to cover metabolic needs. The nitrogen equivalent of as much as 300 grams of protein can be administered intravenously each day.[25,44]

Casein hydrolysates are a more concentrated and cheaper source of protein than plasma or whole blood, and have the additional advantage of containing less sodium; therefore, they are safer to administer to patients with cardiac or renal impairment. Pure amino acids are as yet difficult to make and are expensive.[21]

NITROGEN BALANCE AFTER IRRADIATION IN NONMALIGNANT DISEASE

No references were found that described the effect of irradiation on the nitrogen metabolism in man in health or in the absence of malignant disease, all experiments having been performed on laboratory animals. Edsall and Pemberton,[17] in 1907, treated healthy dogs to the point of radiation sickness and noted an increase in nitrogen output and blood nonprotein nitrogen. Pohle and Sevringhaus[34] exposed 14 dogs to 500 r in air and failed to find any characteristic change in the hemoglobin, total nonprotein nitrogen, uric acid, sodium chloride, or cholesterol in blood. They did not do nitrogen balance studies. Davy[15] exposed 9 healthy dogs to 500 r. Almost all showed a regular though slight diminution of serum albumin within forty-eight hours, with the decrease beginning almost immediately and returning to normal in twenty-four hours.

Hall and Whipple[23] found that normal dogs treated to the point of radiation sickness developed an increase in urinary nitro-

gen and blood nonprotein nitrogen twenty-four hours after exposure, lasting until death. This change was associated with increased excretion of purine bases and phosphorus.

NITROGEN BALANCE IN MALIGNANT DISEASE

Studies on nitrogen metabolism in malignant disease in man are early and historic. The first American writer on the subject was D. L. Edsall,[18] who in 1905 reported studying nitrogen balance in a patient with acute leukemia who had a nitrogen intake of 7.25 grams and an output of 29.5 grams in twenty-four hours. He quotes Magnus-Levy, who described 3 similar cases with negative nitrogen balance.

Musser and Edsall,[30] in 1905, also reported the trend of nitrogen balance in 2 cases of leukemia before and after radiation therapy, showing a variable effect.

Murphy, Means and Aub,[29] in 1917, followed the nitrogen balance of a patient with lymphatic leukemia and found it to vary from plus 0.8 to plus 3.3.

Goldman[22] followed the nitrogen balance in 12 patients with malignant disease receiving 200 kv. radiation therapy and found negative nitrogen balance during and shortly after irradiation. The nitrogen loss was greater in patients with radiosensitive tumors. The site of irradiation had no influence on nitrogen metabolism. Eventually, nitrogen balance returned to positive. Similar changes were reported by Robertson[37] using radiations generated at 1,000 kv.

METHOD OF EXPERIMENT

Selection of Cases. In the present study, observations were made on 25 patients at the State University of Iowa Hospitals in Iowa City, Iowa (Table 1), for an average period of twenty-five days. Cases were selected by the following criteria:

1. Limited avenues of nitrogen loss. Cases with hemorrhage, exudation, ascites or edema were excluded. Two patients developed edema and 1 ascites at the termination of the course of the study, and values during that period were omitted.

2. Advanced malignant disease. Extensive local involvement or distant metastases were present in all cases except 1, a well nourished patient in which adenocarcinoma of the ovary was grossly completely removed and the patient was receiving prophylactic roentgen therapy. Clinical cachexia was present in 15 individuals and was indicated by evidence of present and previous weight loss. Ten were well nourished.

3. Absence of involvement of the gastrointestinal tract. This limitation was set to minimize the factor of impaired absorption of nourishment. Included in the series were 2

TABLE I

DISTRIBUTION OF CASES BY DISEASE AND NUTRITION

Diagnosis	Cachectic	Well Nourished	Total
Carcinoma of the breast—recurrent or metastatic		3	3
Hypernephroma with metastases	1	1	2
Carcinoma of hypophyarnx with metastases		1	1
Malignant lymphoma (leukemia, Hodgkin's disease)	3	1	4
Pancreatic carcinoma with metastases	2		2
Carcinoma of tongue—recurrent	2		2
Carcinoma of the cervix—recurrent or metastatic	4	2	6
Carcinoma of the parotid gland with metastases	1		1
Carcinoma of the testes with metastases		1	1
Carcinoma of the sigmoid colon	1		1
Carcinoma of the ovary, grossly completely excised		1	1
Carcinoma of the lung with metastases	1		1
Total	15	10	25

patients with carcinoma of the tongue, 1 carcinoma of the hypopharynx and 1 carcinoma of the sigmoid colon, 2 carcinomas of the pancreas, and 1 carcinoma of the parotid gland, as it was felt that lesions in these areas would not interfere with food absorption.

4. Good patient cooperation. Patients who were incontinent were excluded from the series. Patients were told to save complete urine and fecal specimens daily if they were ambulant, and efforts were made to select subjects who appeared to be dependable. Nurses made collections for bedfast patients. When lack of patient or nurse cooperation was suspected, the case was abandoned.

Method of Determination of Nitrogen Balance. The oral nitrogen intake was based on the measurement of ingested protein and was calculated by a nutrition intern, who weighed the submitted and returned food. The total protein present in the so-called regular hospital diet contains 11.2 grams of nitrogen, and this value was arbitrarily chosen as the division point between a low level and a high level of nitrogen intake.

The nitrogen in the hydrolyzed protein employed runs uniformly at 8 grams per 1,000 cc. The nitrogen in the plasma protein of transfused blood was calculated at 3.2 grams per 500 cc. Total nitrogen intake consisted of the sum of the oral and parenteral nitrogen.

Complete twenty-four collections of urine were made daily during the course of observation and nitrogen content determined by Kjeldahl's method. Total stool specimens for three to six days were merged and average daily values computed. In the absence of gastrointestinal disease, the fecal nitrogen remains steady over a long period, since it is entirely constituted by the nitrogen content of fecal bacteria. The average value for the sample period was accepted as the daily value for the individual during the entire course of study.

RESULTS OF INVESTIGATION

This study indicates that the nitrogen intake is the principal factor regulating nitrogen balance (Table II). Fifteen out of 17 patients receiving over 11.2 grams of nitrogen daily were in positive balance, while 7 out of 8 of those receiving less were in negative balance. The nutritional state was the factor conditioning the nitrogen intake.

TABLE II

NITROGEN INTAKE AND NITROGEN BALANCE

Dietary Level	Number of Cases	Average Daily Nitrogen Intake	Nitrogen Balance
Low level nitrogen intake	8	6.1	−1.0
High level nitrogen intake	17	16.9	+4.7

All well nourished patients easily accepted a high level of protein intake, but the cachectic patient did so with difficulty. Of 15 cachectic patients, only 7 achieved a high level of nitrogen intake, including 5 who did so with the aid of intravenously administered protein hydrolysates.

However, cachexia is not simply a matter of anorexia preventing an adequate nitrogen intake. All but 3 of 16 cachectic patients had nitrogen intakes in excess of minimum daily requirements for nitrogen maintenance of healthy active individuals (Table III), but unless they consumed practically all the nitrogen present in a high protein diet, cachectic patients continued to lose nitrogen (Table IV). The rate of nitrogen loss increased with increased nitrogen intake until a threshold was passed, after which these patients could achieve a positive equilibrium (Table V). Extravagant quantities of nitrogen were required to produce anabolism in the cachectic

TABLE III

ACTUAL DAILY NITROGEN INTAKE COMPARED TO CHITTENDEN STANDARD FOR NITROGEN MAINTENANCE IN HEALTH

Nutritional Status	Number of Cases	Required Daily Nitrogen	Ingested Daily Nitrogen	Average Nitrogen Balance
Cachectic	10	6.9	7.9	−1.1
Well nourished	8	7.9	16.2	+5.1

Note: (1) Patients receiving parenteral nitrogen excluded from series. (2) Calculation of required daily nitrogen based on upper value of range of Chittenden standard.

TABLE IV

NITROGEN BALANCE AND NUTRITIONAL STATE

	Cachectic			Well Nourished		
	No. of Cases	Average N/D	Average Nitrogen Balance	No. of Cases	Average N/D	Average Nitrogen Balance
Low level oral nitrogen intake	8	6.0	−1.0			
High level oral nitrogen intake	2	15.2	−1.7	8	16.2	5.1
High level nitrogen intake, oral and parenteral combined	5	18.3	5.6	2	14.8	6.6

group. This phenomenon occurred to the same degree in both irradiated and non-irradiated patients.

The explanation of this paradoxical action is not clear. It may lie in the nature of the unknown process which precipitates cachexia. Ariel[5] has hypothesized an agent inhibitory to protein synthesis, present as part of the generalized effects of malignant disease. The lowest urinary nitrogen occurs in starving individuals. Perhaps feeding the malnourished patient increases the activity of this agent until the nitrogen intake passes a certain level at which the catabolic effect is overwhelmed and the individual enters an anabolic phase.

In well nourished patients, the higher the nitrogen intake, the better was the utilization of nitrogen. These patients were able to maintain a high grade of nitrogen retention on a lower nitrogen intake than those cachectic patients forced into positive nitrogen balance (Table v).

The trend of nitrogen balance in cachectics who were forced into nitrogen retention and then permitted to return to a diet of their own choice is not known. Although knowledge of this course is of practical importance, circumstances prevented the long term observation of more than 2 patients in this category. These patients were examined sixteen and fifty-two days respectively following cessation of the special high nitrogen diet. During the interval their diet was not controlled. Both patients showed an eventual drop in plasma protein and plasma albumin concentration.

The Effects of Intravenous Hydrolysates. Individuals receiving protein hydrolysate intravenously were always in positive nitrogen balance during the period of administration. This consistently occurred in both cachectic and well nourished patients (Table iv). It is important that hydrolyzed protein given intravenously be delivered slowly to prevent dumping of amino acids into the urine. When this is done, it is well utilized, and on a plane comparable to that of an oral high protein diet. The

TABLE V

RELATIVE EFFECT OF NITROGEN INTAKE ON NITROGEN BALANCE

Grams Average Daily Nitrogen Intake

	0–5		5–10		10–15		15–20		20–25	
	No. of Cases	Nitrogen Balance	No. of Cases	Nitrogen Balance	No. of Cases	Nitrogen Balance	No. of Cases	Nitrogen Balance	No. of Cases	Nitrogen Balance
Cachectic	3	−0.3	5	−1.5	1	−2.0	5	4.9	1	2.5
Well nourished					5	3.2	4	7.1	1	9.8

urinary and fecal nitrogen did not vary whether protein was given orally or parenterally (Table VI).

When patients received Amigen intravenously, the amount of protein taken orally was curtailed and the appetite for all types of food was reduced. It is significant that the nitrogen intake of patients receiving high protein diet and Amigen exceeded that of patients on high protein diet alone by an average of only 1.3 grams per day.

Creatinine values fluctuated widely within the same individual from day to day despite collection of complete urine specimens. Average values varied from 0.20 to 1.20, the higher excretion rates occurring after roentgen therapy, corroborating the findings of others regarding increased purine output in urine following irradiation.[12,16,34] No relationship could be derived between creatinine output and nutritional state, diet or nitrogen balance.

Conservation of nitrogen occurred in all cachectic patients on a low nitrogen intake, the urinary fecal nitrogen being two-thirds that of patients on a high nitrogen intake (Table VI).

Roentgen therapy uniformly caused a slight increase in urinary nitrogen, but to a lesser degree in cachectic than in well nourished individuals.

Of 5 cachectic patients receiving hydrolyzed protein intravenously, 1 developed edema and 2 ascites during the period of administration. Positive nitrogen balance was established prior to rapid weight gain. Early nitrogen accrual indicated tissue synthesis, but toward the end of the period, it indicated the pooling of extracellular fluid. Although in each instance the spread of neoplasm could account for the development of edema and ascites, these effects were probably the result of restoration of fluid balance in chronically dehydrated individuals with masked depression of plasma albumin levels. In each instance, the plasma albumin level fell steadily with hydrolyzed protein administration. In 2 well nourished individuals receiving hydrolyzed protein, edema did not develop and the plasma albumin levels remained unchanged.

Effect of Treatment of Nitrogen Balance. Included in this series were 3 cachectic individuals in the terminal stages of advanced malignant disease who were receiving only supportive therapy. Despite a very low nitrogen intake, these patients were almost in neutral balance, 2 being slightly negative and 1 being positive enough to swing the average to the plus side. Although the evidence of progressive protein depletion was obvious in these patients, the rate of nitrogen loss was minimal during the period of observation, and was probably at a low ebb due to the conserving action of the body economy. Of the remainder of the patients receiving supportive treatment only, well nourished and cachectic patients on a high level of nitrogen intake were all able to deposit large quantities of nitrogen (Table VII).

Seventeen patients received courses of irradiation for periods of from three to sixty days, the average duration of treatment being fifteen days. A drop occurred in the average nitrogen balance of all groups receiving treatment. The cachectic patients

TABLE VI

EFFECT OF DIET ON NITROGEN OUTPUT

Dietary Type	No. of Cases	Nitrogen Intake	Urine Nitrogen	Fecal Nitrogen	Total Nitrogen Output
Low level oral nitrogen	8	6.1	6.7	0.8	7.5
High level oral nitrogen	10	16.0	10.4	1.3	11.7
Oral and parenteral nitrogen combined	7	17.3	10.2	1.2	11.4

were placed into negative nitrogen balance. The well nourished patients remained in positive balance, but the margin was decreased, a greater relative depression occurring than in the case of cachectic individuals. This trend persisted in patients of both nutritional states receiving intravenous protein hydrolysates (Table VII).

DISCUSSION

It has been generally assumed that the development of cachexia is associated with negative nitrogen balance. This study tends to confirm that belief. The nitrogen deficit could be demonstrated only in patients with a clinical degree of cachexia, the well nourished patients remaining in positive nitrogen balance.

Irradiation has a depressing effect on nitrogen balance in both well nourished and malnourished patients. The increased nitrogen output is believed to be due to breakdown of protein in tissues limited to the area of irradiation.

In cachectic patients the nitrogen loss was further stimulated by increasing the nitrogen intake up to a threshold. Beyond this level positive nitrogen balance could be established. The level of this threshold is not known, but it is surpassed in cachectic patients by tripling the average protein intake of the cachectic patient. In this manner, even cachectic patients will retain protein, at least for the length of the period of administration of a high level nitrogen intake.

In this series, all well nourished patients with malignant disease were in positive nitrogen balance. Nitrogen deposit apparently was related to the high level of nitrogen intake common to the group. While not all individuals on a high level of nitrogen intake were in positive balance, in all but 2 out of 17 cases this diet induced positive nitrogen balance even in cachectic individuals.

TABLE VII

EFFECT OF TREATMENT ON NITROGEN BALANCE

		No Treatment		Radiation Therapy	
		No. of Cases	Nitrogen Balance	No. of Cases	Nitrogen Balance
Cachectic	Low level nitrogen intake	3	0.1	5	−1.8
	High level nitrogen intake	4	5.6	3	0.9
Well Nourished	Low level nitrogen intake	0		0	
	High level nitrogen intake	1	9.8	9	4.9

While the cause of the change from the well nourished to the cachectic status is not known, its onset can be recognized by weight loss. As body weight is dependent in part on water balance the state of hydration may confuse the picture. The most accurate index of the onset of cachexia and its rate of progress is the nitrogen balance study, and this is suggested as a consideration in the evaluation of the status of a patient with extensive malignant disease.

Whether cachexia, in retarding the rate of the physiological processes, prolongs or shortens the life of the cancer patient is not known. Beneficial effects such as restoration of tissue proteins, with resultant regeneration of hemoglobin, antibodies, and enzymes are known to occur with im-

proved nutrition. However, the effect of increased nitrogen intake on the tumor must also be considered. Experiments on laboratory animals show that increased nitrogen consumption leads to increased rate of tumor growth.[47] Morton[28] found that tumor tissue has a greater priority for protein than does normal tissue. Conversely, retardation of the growth rate of tumors in cachectic individuals is a common observation.

In this series, there was no accurate index by which to gauge tumor growth, nor was the period of observation long enough to be significant. There was no grossly observable acceleration of tumor growth among any of the patients on high nitrogen intake in this series.

Many radiologists have observed an increased radiosensitivity of tumors in well nourished as compared to malnourished individuals. That well nourished individuals can withstand intensive courses of irradiation better than malnourished is well known. Often, the presence of cachexia is the limiting factor preventing the administration of a cancerocidal dose of radiation.

It would appear that if the administration of a high level of nitrogen intake will inhibit or forestall cachexia, it might be of value in improving the effectiveness of radiation treatment and prolonging the life of the patient with extensive malignant disease.

SUMMARY

The number of cases in this series is too small to warrant definite conclusions but the following tendencies are indicated:

1. In patients with malignant disease, the cachectic process is associated with negative nitrogen balance. Well nourished patients are in positive nitrogen balance.

2. Cachexia can be reversed by the administration of a sufficiently high nitrogen intake. Increased nitrogen intake below this level induces greater negative nitrogen balance.

3. Anorexia appears to be the effect rather than the cause of negative nitrogen balance.

4. Radiation therapy induces a drop in nitrogen balance in both well nourished and cachectic individuals, the greater degree occurring in the former group.

5. Conservation of nitrogen is observed in cachectic patients, reaching its highest degree as the cachexia becomes extreme.

6. The nitrogen balance study affords a method of evaluating the status of the patient with advanced malignant disease.

7. Patients with advanced malignant disease should receive protein far in excess of that afforded by the regular hospital diet, in order to maintain nitrogen balance. This is especially true when the patient is receiving radiation therapy.

8. The possibility of prolonging the survival of patients with advanced malignant disease by improving their nutrition is suggested.

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Acknowledgment is made to Dr. Katherine Daum, Director of the Department of Nutrition at the State University of Iowa Hospitals, in whose laboratory the chemical analyses were made, and who personally determined numerous values; to the Mead Johnson Company, which furnished the protein products, Protenum protolysate and Amigen; to the Department of Radiology of State University of Iowa Hospitals which supplied a grant making the study possible; and to H. Dabney Kerr, M.D., who aided in the preparation of this paper.

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DESCRIPTION OF A CONE WITH A MOVABLE GRID FOR GRID THERAPY

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A SPECIAL cone was designed to facilitate the correct placement of a movable grid for depth dose measurements and for therapy. The grid is made of lead instead of lead rubber so that only a small fraction of the incident beam is transmitted through the covered part. The grid is inserted into the base and easily moved in any direction in this plane.

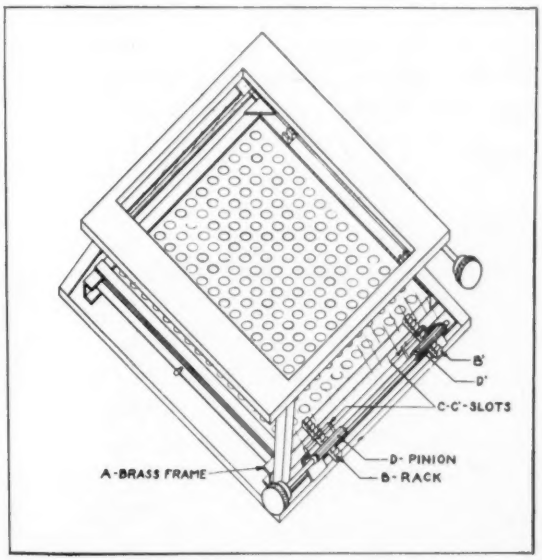

FIG. 1. Isometric drawing of the cone.

Figure 1 is an isometric drawing of the cone. Three sides of the cone and the bottom are made of lucite with the corners reinforced with brass; the fourth side is open. Through this side of the cone, the grid is inserted into a brass frame *A* which rests on the lucite bottom. A pair of racks *BB'* is attached to each of two adjacent sides of the frame and protrudes through slots *CC'* cut in the sides of the lucite cone. A pinion arrangement *D* moves the racks so that the frame with the grid in it can be moved in any direction in the plane of the bottom. The pinion must be at least as wide as the desired motion of the grid, in our case 14 mm., or the distance between the centers of the openings in the grid. A greater motion than this would be preferable. Figure 2 is a photograph of the cone looking down from above.

Any grid or diaphragm can be placed in the frame. The grid which we used was made of a lead sheet 5 mm. thick fastened to a sheet of aluminum 2 mm. thick to absorb the characteristic radiation of lead and give it rigidity. (A sheet of aluminum 1 mm. thick would have done as well.) This grid transmits 1.6 per cent of the incident beam whose half-value layer is 3.3 mm. Cu.

The movable grid can only be used when there is a light device to show the position of the beam.

In making depth dose measurements the chamber can be placed under a hole by moving the grid until the circle of light is

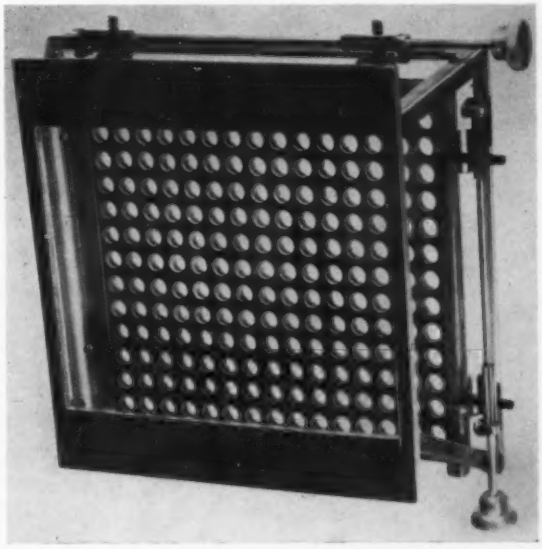

FIG. 2. Photograph of the cone looking down from above.

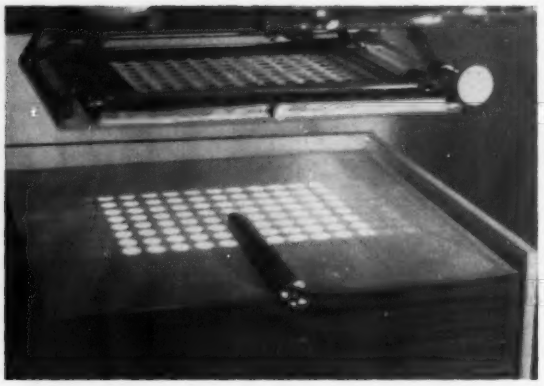

FIG. 3. Ionization chamber, under an opening, in light spot, in a presdwood phantom.

FIG. 4. Light pattern of the grid showing the "spots" on a patient.

over the chamber or the chamber can be placed under the covered portion by moving the grid until the chamber is in the shadow of this portion. Figure 3 shows a presdwood phantom with the chamber under an opening. The chamber can be covered with the required thickness of presdwood.

In some cases, because of body curvature, the grid cannot be placed directly on the patient. When this obtains, the following procedure is used. With the field of the patient as parallel to the cone as possible at a fixed distance, limited only by the ability to apply the markings for the spots, the "spots" are marked to correspond to the centers of the circles of light coming through the openings. The cone is then brought down on the patient. The next time the patient is set up, the light field with the grid removed is superimposed on the field as marked on the patient's skin. The grid is then placed in the frame with the cone at the same distance as was used previously. The grid is moved until the circles of light are over the spots. Figure 4 shows the circles of light on the spots as marked on the patient. The cone is then brought down to the skin. The grid pattern obtained on patients with the grid used in this way was fairly good. Care must be taken in arranging the patient the same way each time.

The motion in two directions can be applied in other than grid therapy. For example, a diaphragm system can be moved in cones with the great advantage of easily positioning the beam on the required part of the lesion.

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Mr. H. B. Odmann devised the mechanism for moving the grid and built the cone as designed.

I wish to thank Dr. J. R. Freid, Chief of the Department of Radiotherapy, who is working on the problem of grid therapy, for his interest and encouragement.

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ABDOMINAL COMPRESSION

THE ALL-IMPORTANT FACTOR IN EXCRETORY UROGRAPHY

By J. W. GROSSMAN, M.D.,* *and* BRODIE C. NALLE, Jr., M.D.†

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A STUDY of the technical factors in excretory urography has been undertaken, and the following conclusion reached. If there is adequate renal function and the technique of film exposure and processing is of high caliber, then the most important factor in the production of excretory urograms of excellent quality is adequately and correctly applied external abdominal pressure. The purpose of this pressure is to temporarily obstruct the ureters. Excretory urograms are thus obtained in which the visualization of the renal pelves and ureters is comparable to that obtained by the retrograde method.

The factors peculiar to excretory urography studied were:

1. Starvation and dehydration
2. Bowel cleansing
3. Quantity of contrast medium employed
4. External abdominal compression

We found that dehydration and starvation are not necessary and that bowel preparation is not essential, and eliminated these forms of preparation. Excretory urography is performed without any preparation of the patient. Both diodrast and neoiopax are used. In the average adult (except extremely obese persons) 10 cc. of contrast medium is usually adequate. Good urograms have been obtained in adults with as little as 4 cc. of 75 per cent neoiopax. The reason for using small amounts of contrast medium was to convince ourselves that the ureteral compression was the all-important factor in obtaining good urograms.

A brief description of the technique of compression follows (see Fig. 1). Articles used are a folded sheet, a blood pressure cuff, and a sphygmomanometer. The lower edge of a folded sheet is placed close to the level of the anterior superior iliac spine, and the blood pressure cuff is placed on top of this transversely. The blood pressure cuff and sheet are held in place by the compression band of the roentgenographic table. The cuff is then inflated to 40–60 mm. mercury pressure for the average person and 60–80 mm. pressure for a heavier person. In most instances this is tolerated by the patient, and any discomfort is compensated by the excellent urograms which result. It requires more pressure to obstruct the left ureter than the right.

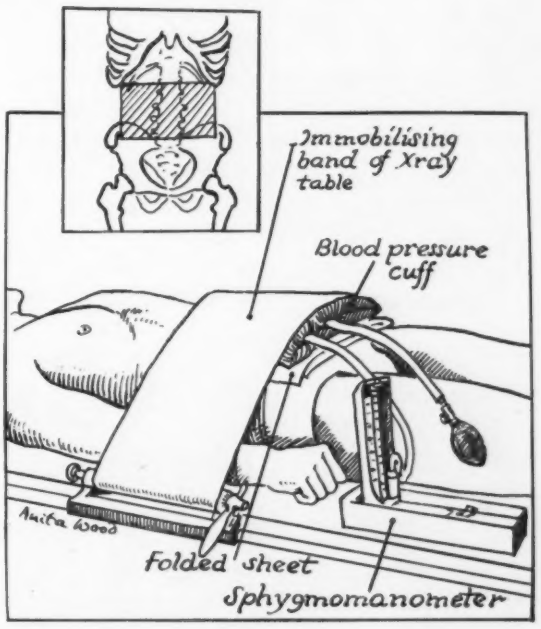

Fig. 1

The following roentgenograms are usually taken: first, a survey film of the urinary tract without pressure; then external abdominal pressure is applied, the contrast medium injected, and films exposed at

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eight, fifteen, and twenty-five minutes following the injection. These are taken with the patient in a 12 degree Trendelenburg position. The patient is then placed in an upright position, the compression device is removed, and a film exposed. This is followed by films of the bladder before and after micturition.

When compression is adequately and correctly applied, the eight, fifteen, and twenty-five minute films show the renal pelves and proximal half of the ureter to a point just above the crest of the pelvis. The pelves become progressively more opaque on each film and usually show up best on the twenty-five minute film. Occasionally, if the compression is not adequate to block the ureter temporarily, some of the contrast medium may leak past the point of pressure, and the distal ureter show on some of the films made with the compression device in place. The upright film shows the distal half of the ureter.

The chief advantage of this method lies in the excellent urograms usually obtained. It also frequently affords excellent visualization of the distal ureters. This results from opaque urine being kept out of the bladder by the temporary obstruction of the ureters during the time the abdominal compression is applied. It enables one to use much less contrast medium in the examination, which may result in fewer untoward reactions; however, we have no proof of this.

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THE CASSETTE VISUALIZER WITH TRANSPARENT TABLE TOP

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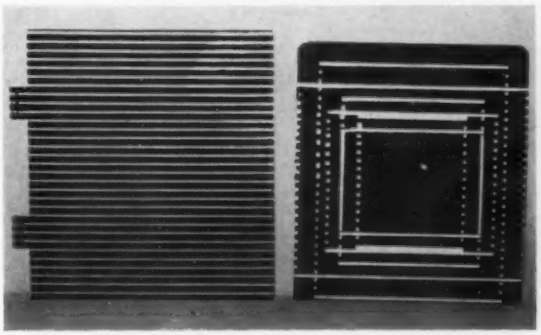
WITH the present methods of positioning patients to cassettes using the movable Potter-Bucky grid, resulting roentgenograms are frequently unsatisfactory. Even with well trained personnel, it has been necessary for the technician to rely on personal judgment to position the part to be examined over a cassette hidden in the Potter-Bucky tray. When persons with little experience or inadequate training do the roentgenography, the results are even more unsatisfactory.

To obviate practically all guesswork in positioning, a new method has been devised by the authors which incorporates a system of outlines corresponding to the exact size and position of the underlying cassettes. These outlines are viewed through a transparent table top which allows direct visualization. A device is also added which permits only the longitudinal or transverse outline of the desired cassette size to be viewed. This eliminates confusion which might result from a multitude of outlines.

CONSTRUCTION

The table top used is a single sheet of transparent "Lucite" (HC-202). The length and width are exactly the same as the conventional plywood top. The thickness of the transparent top is $\frac{1}{2}$ inch. It has been shown by mathematical computation and proved by actual test that this thickness is of sufficient strength to support a 300 pound patient with no more sag than that occurring with conventional tops. It has also been proved experimentally that this thickness has sufficient radiotransparency and will in no way affect the technical quality of the roentgenograms made through this material.

On the pilot model the system of outlines of the various sized cassettes were painted in white on a black cardboard background (Fig. 1*B*). This cardboard was fitted snugly to the top of the movable Potter-Bucky grid (Fig. 2*A* and *B*). The outlines were centered to the underlying cassettes with the Potter-Bucky grid in the uncocked position. This is the "resting" position of the Potter-Bucky grid in tables where the mechanism is either of the automatic reciprocating or manual type. A line-mask device (Fig. 1*A*) is used to reduce confusion due to multiple lines. The line-mask is composed of a thin, transparent plastic sheet equal to the dimensions of the surface of the Potter-Bucky grid. Black strips were painted on the plastic surface at regular intervals resulting in alternate opaque black and transparent zones. By making the outlines on the cardboard interrupted blocks instead of



A B

FIG. 1. (*A*) Line-mask device with alternate transparent and opaque black strips. (*B*) Cardboard with outlines corresponding to cassette sizes and positions.

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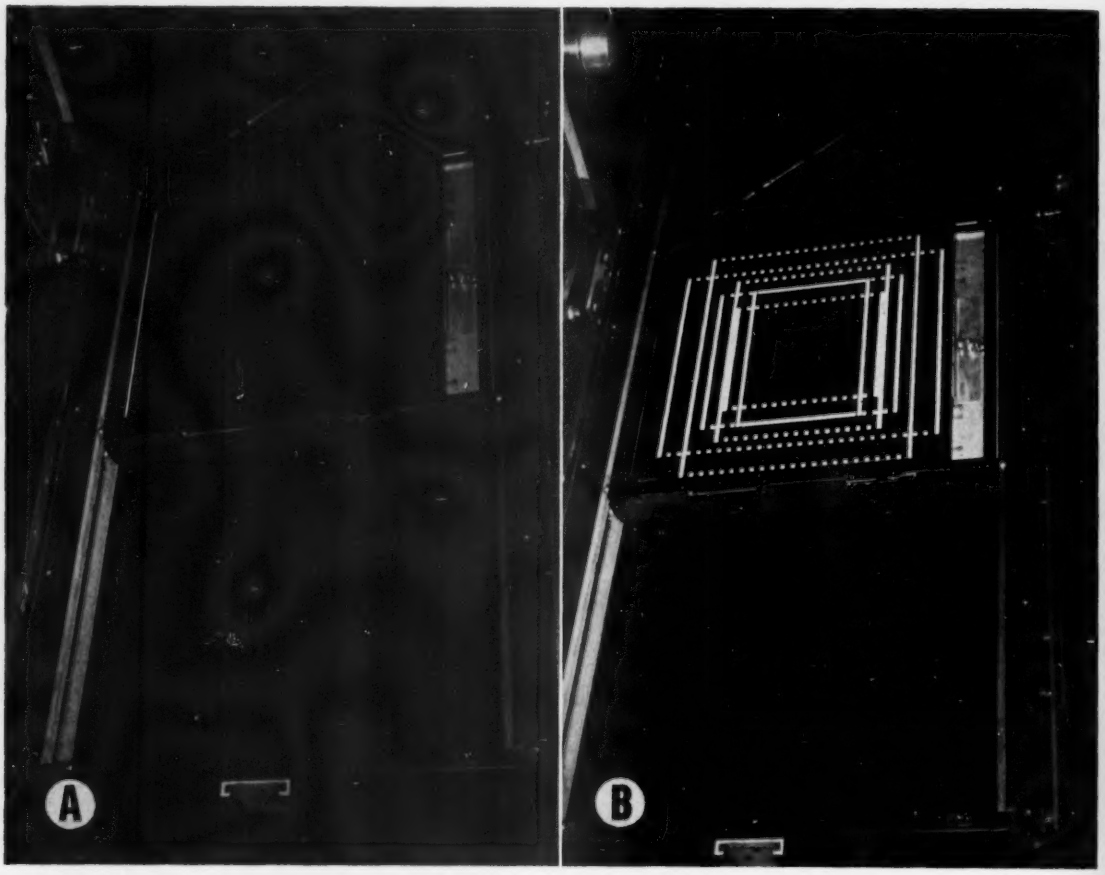

Fig. 2. (*A*) Roentgen table showing top of Potter-Bucky mechanism. (*B*) Same with cardboard marked with outlines mounted on top of Potter-Bucky grid.

solid lines and by moving the overlying line-mask a short distance, some lines can be made to disappear and others appear (Fig. 3*A* and *B*).

As can be seen in Figure 4, the principle is simple yet highly effective and readily adaptable to the more complex outlines.

Because this device is attached to the Potter-Bucky grid, the outlines are always in the same position as the cassettes. Hence, both the Potter-Bucky grid and the cassette visualizer can be rolled to any position on the table. The mechanism for moving the line-mask is conveniently located under the edge of the table top where it is easily reached by the technician. A shift of less than 1 inch is necessary to make a "change" in the direction of the outlines. Because only the line-mask moves during this change, the outlines remain exactly centered over the cassette underneath.

SUMMARY OF ADVANTAGES

This new device offers many advantages. The outline corresponding to the exact size and position of the underlying cassette can be visualized directly through the transparent table top. This makes positioning almost foolproof (Fig. 5). Because the device remains permanently attached to the Potter-Bucky grid it may be positioned at any place along the table simply by moving the film tray. Centered outlines of all cassette sizes in both the longitudinal and transverse positions relative to the table are provided. The device can be used with equal ease when the table is in the upright or hoizontal position. The plastic

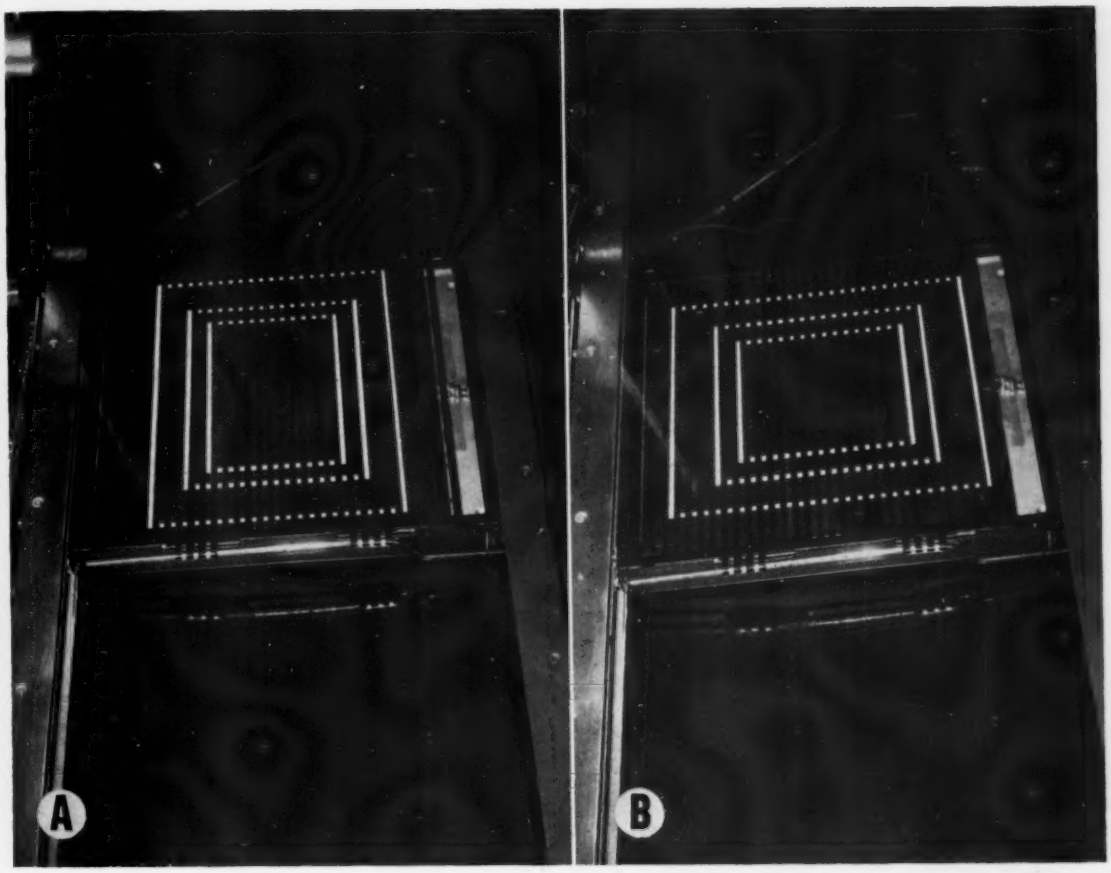

Fig. 3. (*A*) Line-mask in place over outlines. Only cassette outlines in vertical position visible through transparent lucite top. (*B*) Same but after shift of line-mask. Only cassette outlines in horizontal position visible through transparent lucite top.

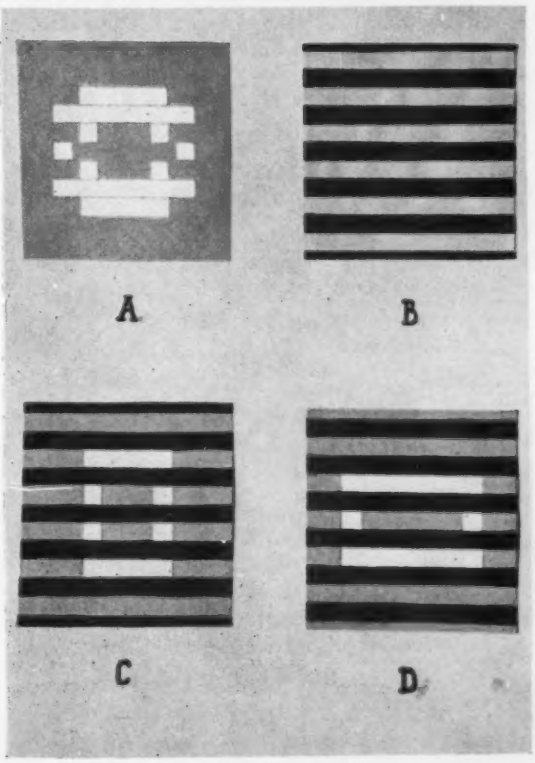

Fig. 4. Simplified model. (*A*) Appearance of outlines in background. (*B*) Line-mask sheet of alternate transparent and opaque strips. (*C*) Position of outline with line-mask over outlines (*A*). (*D*) After movement of line-mask down slightly, horizontal outline now visible.

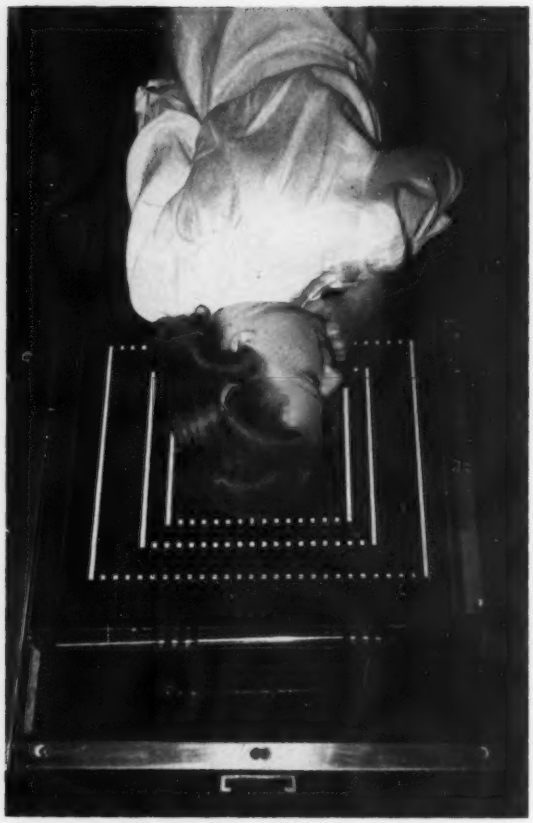

FIG. 5. Photograph showing relationship of patient for lateral skull exposure to 10 by 12 inch film outlined by the "cassette visualizer." The cassette visualizer is in its horizontal position.

table top used in the construction has adequate strength, is sufficiently radiotransparent and is easily cleaned. To prevent scratching of the surface it is well to cover the top with a sheet of transparent film base. Expense of reëxamination would be reduced because exact centering would eliminate unsatisfactory films. The training of roentgen technicians would be simplified by the ease of centering provided. The device is easily installed in existing equipment and would require a minimum of redesigning of new equipment. The construction is simple and rugged which should provide long trouble-free service.

CONCLUSION

An object to film positioning device (the cassette visualizer) used with a transparent plastic table top is described which offers many advantages over existing methods of positioning.

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Milwaukee 3, Wisconsin

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Thirty-fifth Annual Meeting: Chase Hotel, St. Louis, Mo., April 20, 21 and 22, 1953.

EDITORIALS

COARCTATION OF THE AORTA

OUR knowledge of the roentgenographic appearance of congenital malformations of the heart and great vessels has been tremendously advanced within the last few years. This has been brought about by the fact that surgical correction of many of these congenital abnormalities is made possible following the excellent work of that great group of splendid surgeons interested in thoracic surgery and particularly in blood vessel surgery.

Among the anomalies of the great vessels is coarctation of the aorta. The pathologico-anatomic knowledge of this has been known since Meckel reported his first case in 1827. A little over one hundred years later, the roentgenological findings of rib notching in aortic coarctation was described by Rösler, and in the following year an independent description of this roentgenographic finding was given by Railsback and Dock. Since the time of these roentgenological descriptions it was thought that rib notching was pathognomonic of coarctation of the aorta; however, within recent years a sufficient amount of evidence has accumulated to show that rib notching may be associated with other conditions. It has been observed in neurofibromatosis, in vascular malformations of the thoracic wall, in tetralogy of Fallot, in aortic valvular disease, in obstruction of the superior vena cava associated with tortuous intercostal veins, and it has also occurred without a specifically proved cause. However, Bruwer and Pugh state that despite this array of additional causes of rib notching, one is safe in saying that it is still the most common and important roentgenologic sign of coarctation of the aorta in the routine film studies of the chest.

Bruwer and Pugh, in their recent paper on "A neglected roentgenologic sign of coarctation of the aorta" point out that besides rib notching, as has been shown by other observers as well as themselves, additional roentgenographic signs of coarctation that have been described include the following manifestations: (1) inconspicuous ascending aorta; (2) dilatation of the ascending aorta; (3) hypoplastic aortic arch; (4) visualization of the site of coarctation in the left anterior oblique position, either at roentgenoscopy or in the roentgenograms; (5) alterations of contour of the barium-filled esophagus that correspond to the coarctate segment or to dilatation of the left subclavian artery, or to poststenotic dilatation of the aorta; (6) prominence of the left border of the superior mediastinum in the posteroanterior roentgenograms, and prominent pulsation of this region when observed roentgenoscopically or recorded kymographically. This prominence of the left border of the superior mediastinum is usually attributed to the dilated left subclavian artery, and lastly (7) direct demonstration of the coarctate segment by means of angiocardiography or direct or retrograde aortography.

In their paper discussing a neglected roentgenologic sign of coarctation of the aorta, Bruwer and Pugh point out that the signs listed above, other than notching of the ribs, have certain drawbacks, namely requiring special examinations or special techniques, and in view of that they reemphasize an additional sign of coarctation of the aorta which is frequently present in routine posteroanterior roentgenograms of the thorax. This sign of coarctation is usually accompanied by some degree of rib notching, in which case, as they say, it is

merely of corroborating value. But they have observed that in some cases rib notching is not present of sufficient importance to suggest coarctation of the aorta in the routine posteroanterior roentgenograms and for this reason they have considered it justifiable to draw attention to an altered appearance of the descending aorta as shown in the posteroanterior roentgenograms in the hope that this sign will be more frequently utilized in arriving at a diagnosis of coarctation of the aorta.

As is well known to all roentgenologists, if a posteroanterior roentgenogram of the thorax is properly exposed, the descending aorta can be well visualized, and normally if the left border of this vessel is traced proximally from below it will be seen to sweep gently into the left margin of the aortic arch as is well shown in all normal roentgenograms of the chest.

Bruwer and Pugh, in an analysis of 97 cases of coarctation of the aorta in the routine posteroanterior roentgenograms, found an altered appearance of the descending aorta in 34 cases. In 29 of the 34 cases some degree of rib notching was present but in 5 of the cases examined there was no evidence of rib notching. In the 34 cases which they examined in the routine roentgenograms of the chest exposed in the posteroanterior projection if the left border of the descending aorta is traced proximally, it can be seen that this border does not sweep gently into the aortic knob when the latter can be well distinguished but that before this line joins the region of the aortic knob, an indentation toward the right is noted just above the level of the left main pulmonary artery. This indentation may be very slight or may be so marked as to give an overlapping double contour. They concluded that it would appear that the degree to which this indentation can be seen depends on a number of factors, namely:

1. The proximity of the origin of the left subclavian artery to the coarctation. When the left subclavian artery arises close to the coarctate segment, it probably represents the upper curve of double contour, and the more dilated the artery is, the more prominent this segment will be.

2. The size of the aortic knob in those cases in which the left subclavian artery originates at some distance from the coarctate segment.

3. The shortness of the pulmonary ligament and the amount of pull it exerts on the coarctate segment.

4. The extent of the circumference of the aorta involved by the coarctate segment, and at what tangent and vertical angle the roentgen rays strike the region of the superior mediastinum, and the variation of position of the involved structures from one patient to another.

5. The size of the lumen of the poststenotic descending aorta.

They state that the double contour seen in some cases and the indentation seen in all of their 34 cases have been described only occasionally in the literature and have not received the recognition merited.

Gladnikoff, in 1946, called attention to the indentation and stated that it was due to a meeting of the shadows of the dilated left subclavian artery and the descending aorta. Schatzki later, in 1947, mentioned a peculiar type of notching in the upper protion of the descending aorta, and Wolke, as early as 1937, gave a good description of the indentation in the left upper aortic border and thought it to represent the site of the stricture of the aorta. Wolke reported 3 cases, in 1 of which rib notching was not present.

Occasionally the notching may be so marked as to cause a double contour to the left border of the superior mediastinum giving an appearance of a mediastinal neoplasm.

In conclusion, Bruwer and Pugh are in agreement that rib notching is still one if not the most important roentgenologic sign of coarctation of the aorta. However, in about a third of the cases of coarctation of the aorta in which operation was performed at the Mayo Clinic another valuable sign was present on the posteroanterior

roentgenogram, and this consisted of a notch in the left border of the descending aorta just above the level of the left main pulmonary artery. This notch represents the coarctate segment. This sign may be present in markedly varying degrees, depending upon the number of factors discussed. In about 5 per cent of their cases the notch in the left border of the descending aorta just above the level of the left main pulmonary artery was the only definite roentgenographic sign of coarctation as seen in the posteroanterior roentgenographic studies of the chest.

The authors who have reported this sign of notching in the left border of the descending aorta state that it may not invariably be due to full-blown coarctation requiring operation but that it may represent the probability of clinical coarctation and that the extent of the coarctation should then be further evaluated by other clinical and laboratory methods.

Neuhauser, in his paper on "Recent advances in the roentgenographic diagnosis of congenital malformation of the heart and great vessels," points out the fact that an accurate diagnosis of the nature of the malformation cannot be made without a clear understanding of the basic physiologic changes caused by such malformation. It is in just such subclinical cases of coarctation of the aorta that are discussed by Bruwer and Pugh that this dictum holds especially true.

However, Bruwer and Pugh have definitely called attention of the roentgenologist to a neglected roentgenologic sign of coarctation of the aorta which would warrant more careful study of the routine roentgenograms of the chest made in the posteroanterior projection.

The brilliant chapter that is being written in the surgical treatment of anomalies of the heart, the aorta and its vessels imposes an added responsibility upon the roentgenologist in the recognition of these anomalies in the routine studies of the chest and, if there are indications, more elaborate roentgenological studies may be carried out to give not only the exact site but the extent of the malformation in the anomalous development.

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PROF. DR. MED. GEORGE FEDOR HAENISCH
1874-1952

THE roentgenologists throughout the world have lost a good friend and a great leader in the death of Prof. Dr. Med. George Fedor Haenisch. He was greatly admired by the radiologists throughout America who had the privilege of knowing him personally. He was particularly friendly to me when I visited Prof. Albers-Schönberg in Hamburg in 1906. He was at that time one of Dr. Albers-Schönberg's assistants. Our close friendship since that date was partly due to the fact that he spoke excellent English. His mother was born in England. His English as well as his German was perfect. We spent a lovely weekend together seeing the sights about Hamburg and discussing the problems involved in roentgenology.

Dr. Haenisch was born August 21, 1874, and received his medical education in Freiburg, München and Strassburg, and served as assistant in surgery under Prof. Helferich in the University Clinic at Kiel, and also as assistant in surgery under Prof. Madelung in the University Clinic in Strassburg.

In 1906, he specialized in roentgenology under Prof. Albers-Schönberg.

In 1910, he was sent as the Official Delegate from the German Röntgen Society to the meeting of the American Roentgen Ray Society held in Detroit, Michigan, and was made an Honorary Member of the American Roentgen Ray Society.

In 1911, he served as Staff Physician in the Military. Also in 1911, he was the Official Guest

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Photograph sent to Dr. Pfahler which was made August 21, 1944, at the celebration and testimonial dinner given by Dr. Haenisch's hospital staff on his 70th birthday.

of the British Medical Association at its meeting in Liverpool.

In 1912, he was Chairman of the Biological Section of the Physicians Congress in Hamburg.

In 1913, he was appointed Chief of the Roentgen Department of the All. Krankenhaus Barmbeck and remained Chief in that Department until his retirement on age, January 1, 1946.

In 1913, he was sent as an Official Delegate to the Section on Roentgenology at the International Medical Congress held in London.

In 1914, he was made Corresponding Member of the New York Roentgen Ray Society.

In 1919, he received the title of Professor from the Hamburger Senat.

In 1923, he was Chairman of the Congress of the German Röntgen Society in München, in honor of Prof. Wilhelm Conrad Röntgen.

In 1923, he was invited to Leningrad, Russia, to lecture in the State Institute for Roentgenology. (After that meeting, he personally reported to me that he had arguments with Prof. Nemenov regarding the socialistic tendencies in roentgenology.)

In 1925, he was Official Delegate from the German Röntgen Society to the First International Congress of Radiology in London.

In 1926, he received the Gold Medal of the Gesolei in Düsseldorf.

From 1927–1933, he served as Permanent Secretary of the German Röntgen Society.

In 1927, he was made Honorary Fellow of the American College of Radiology.

In 1928, he was Official Delegate to the Second International Congress of Radiology held in Stockholm and he was also Official Delegate in 1931 to the Third International Congress of Radiology held in Paris.

In September, 1931, he was called upon to give the Caldwell Lecture before the American Roentgen Ray Society, and received the Society's Gold Medal.

In December, 1931, he was invited to take part in the Congress of the British Institute of Radiology and the British Roentgen Ray Society in London.

In 1932, he was made Honorary Corresponding Member of the Radiological Section of the Royal Society of Medicine in London.

In 1934, he was Delegate of the German Röntgen Society at the Fourth International Congress of Radiology held in Zurich and St. Moritz, Switzerland.

In 1937 he received the Rieder Gold Medal at the Breslau Congress of the German Röntgen Society.

In 1937, he was Official Delegate from the German Röntgen Society to the Fifth International Congress of Radiology held in Chicago, Illinois, and was the Honorary Chairman at the Fourth Session of this Congress and official speaker for Germany.

In 1938, he was the guest of the Italian Medical Radiological Society.

In 1938, he was made Honorary Member of the Roentgen Society of Hungary.

In 1944, he received the Goethe Medal.

In 1950, he was the Official Delegate to the Sixth International Congress of Radiology held in London.

In 1951, he was made Honorary Permanent President of the German Röntgen Society.

In 1951, he was also made Honorary Member of the Spanish Roentgen Society.

From a personal note written to me on November 17, 1946, I quote: "Someone else told me that my death was pronounced in the American Literature. This is up to now not quite right. I am still surviving, although starving is not always very far from us over here. Gertrud was already down to 95 German pounds. But I managed to get her better by the Black Market. I heard you retired lately. I was pensioned in consequence of my age on January 1, 1946. I am still living at my old hospital (Barmbeck) as there is no other lodging to be found. I am occupied all day long partly in the garden, mostly at my writing desk. I just finished the fourth edition of our textbook on roentgenology with Holthusen, and an essay on our results on x-ray treatment of collum carcinoma. I wonder whether you know that my son Rolf stayed in the Black Sea forever. My son, Guenther, is still an American prisoner of war. In 1943, I was operated on for carcinoma metastasis submaxillary. A few days later my private institute was utterly extinguished by air raid and another day later our home in Wentzelstrasse 6 was bombed and burned down to the cellar. Nothing left. Since then I live in my office room at the hospital with Gertrud. In 1945 we had

to leave the Barmbeck Hospital to the Occupation Army and had to take up the Old Garrison Hospital in Wandsbek where I still stay.

"On my 70th birthday I was rewarded by the University with the Goethe Medal and a few years before the German Roentgen Ray Society made me an honorary member and bestowed on me the gold medal. I have nothing more to wish for and am ready to go to the cemetery. It is no more worth while living and starving in Germany after all what happened here."

On his 70th birthday he was given a testimonial dinner. Two years later he retired from his active practice of roentgenology. He continued to serve as co-editor with Prof. Holthusen of the "Fortschritte auf dem Gebiete der Röntgenstrahlen," and in their preparation of the fourth edition of "Einführung in die Röntgenologie."

On February 3, 1948, I received a personal letter from him which shows how much he appreciated the friendship of both the Americans and the British. He said, "The good will to help and the friendly feeling on the great parts of the population in the U.S.A. and England is beyond any doubt."

About five years ago he began complaining of severe pains in his lower spine and radiating down the legs which were believed to be due to a disc lesion between the fourth and fifth lumbar vertebrae. His pains had grown progressively worse during this period and after about ten days of acute illness, he was placed in the hospital and was found to be suffering from acute leukemia, from which he died on December 24, 1952.

He is survived by his devoted wife, Gertrud, with whom he lived happily and who always accompanied him on his visits to the United States, and for whom many of us developed a sincere friendship. He is also survived by one son, one daughter, and two grandchildren.

George E. Pfahler, M.D.

HOWARD Y. PENNELL
1874-1952

HOWARD YARNALL PENNELL, radiologist at the Chester County Hospital in West Chester, Pennsylvania, from 1909 until his death in 1952, was one of the most distinguished members of the medical profession in Pennsylvania. He was born at Wawa, Delaware County, Pennsylvania, July 24, 1874. His early education was at Westtown Friends Boarding School, from which he was graduated in 1892. After a brief period of work at the Academy of Natural Sciences in Philadelphia, he entered the University of Pennsylvania School of Medicine, from which he ob-

tained his degree as Doctor of Medicine in 1898.

After serving the Chester County Hospital as its first intern, in 1899 Dr. Pennell established himself in the general practice of medicine in Downington, Pennsylvania, From the very beginning, he endeared himself to his patients and their families. In spite of the increasing demands upon him in active practice, Dr. Pennell continued his interest in the Chester County Hospital, situated nine miles away, and was a member of the visiting staff.

About 1909, Howard Pennell was granted sufficient funds by the Board of Managers of the Chester County Hospital to equip a somewhat primitive roentgenological department in the basement of the main building of the hospital. At first, he himself carried out every detail of the examinations, including the development of the glass negatives. The success of his pioneer efforts in roentgenology became increasingly apparent by the confidence of the local physicians and surgeons in the accuracy of his scientific work.

In 1929 Dr. Pennell moved, with his wife and daughter, to West Chester, Pennsylvania, and began to devote his entire time to the specialty of radiology. The department at the Chester County Hospital expanded under his direction, with the guidance of those whose opportunities for advanced studies in this field rendered them invaluable as consultants.

Until his death on March 30, 1952, Dr. Pennell was an active member of the Chester County Medical Society, the Medical Society of the State of Pennsylvania, the American Medical Association, and the American Roentgen Ray Society. In the year 1948, he was the recipient of a testimonial for fifty years of service as a physician from the Medical Society of the State of Pennsylvania.

He was a birthright member and a well known minister of the Religious Society of Friends. His community interests included membership on the Board of Managers of the Elwyn Training School, and in the Chester County Historical Society.

In his memory, the radiological department of the Chester County Hospital is to be known as the Pennell Department of Radiology and an annual award of fifty dollars, to be known as the Pennell Award, is to be given to the worthiest intern of the year.

J. Gershon-Cohen, M.D.

SIDNEY LANGE
1879-1952

DR. SYDNEY LANGE was born on October 5, 1879, at Maysville, Kentucky. He died on May 9, 1952, of cerebral hemorrhage. Dr. Lange graduated from the University of Cincinnati with an A.B. degree in 1900. He received his M.D. degree from the Medical College of Ohio at Cincinnati, which later became the College of Medicine of the University of Cincinnati. He interned at the Cincinnati General Hospital in 1904 and spent the year 1905 at the Allgemeine Krankenhaus in Vienna under Professor Guido Holzknecht. He spent his entire professional career in Cincinnati. From 1906 to 1909 he was Lecturer in Electro-Therapeutics at the Miami Medical College in Cincinnati. From 1909 to 1917 he was Lecturer in Roentgenology at the College of Medicine, University of Cincinnati. In 1917 he became Professor of Radiology from which position he retired with the title of Professor Emeritus in 1951. As early as 1906 he was roentgenologist to the Jewish Hospital at Cincinnati. In 1907 he became the roentgenologist to the Good Samaritan Hospital, in 1908 roentgenologist to the Deaconess Hospital, and in 1910 to the Bethesda Hospital. At one time he was also on the Staff of the Booth Memorial Hospital at Covington, Kentucky, and the U. S. Veterans Bureau in Cincinnati. In 1908 he became the roentgenologist to St. Mary Hospital in Cincinnati and maintained a staff position there until the time of his death.

In 1905 Dr. Lange became a member of the American Roentgen Ray Society. In 1913 he was its secretary and in 1914 he was the president of the Society. He was one of the pioneers in roentgenology and in the early years of the specialty's development contributed extensively to the literature. About forty papers were published by Dr. Lange, most of them in the early years. He was the first to utilize the roentgen ray in the diagnosis of diseases of the mastoid. He was also the first to study the phenomenon of enlargement of the thymus gland in infants and the effect of therapeutic roentgen irradiation on it.

Being deeply interested in clinical medicine, Dr. Lange carried on for almost fifty years an extremely active practice in his chosen field. With several exceptions for reason of health, he devoted his entire life and efforts to medicine. A tireless and indefatigable worker, he labored no less than twelve hours a day, seven days a week, with almost no vacations during his entire practice. His last real vacation was in 1934 when he attended the International Congress of Radiology in Zurich, Switzerland. Through an anonymous grant, Dr. Lange was responsible for the establishment of the laboratory at the University of Cincinnati devoted to atomic medicine. It was not until following his death that he was revealed as having been the sole contributor to this laboratory.

With the passing of Dr. Lange, radiology has lost one of its pioneers and early contributors to the development of the specialty.

HAROLD G. REINEKE, M.D.

HARRY HAND McGEE
1901-1952

HARRY HAND McGEE died at Duke University Hospital, November 7, 1952, of general metastases from a bronchogenic carcinoma. He was born in Plains, Georgia, January 5, 1901, the son of Harry Hand McGee and Anna Evans McGee. His father had been a physician of prominence in Savannah, and his own son, Harry H. McGee, is the third generation who has followed a medical career.

Moving to Savannah when young, he was graduated from Savannah High School, and took his pre-medical course at Tulane University. He was graduated in

1924 from the University of Georgia Medical School and took post-graduate training in roentgenology at Jefferson Medical College under Dr. Willis F. Manges.

Harry McGee was a talented man and able practitioner, gifted with a cordial and attractive personality. He enjoyed the approbation and friendship of his associates, and a wide and favorable reputation in and around Savannah. He was roentgenologist to the Central of Georgia Railway Hospital, St. Joseph's Hospital, and at times roentgenologist to the Georgia Infirmary (the oldest such Negro institution in the United States), and to the United States Public Health Hospital.

He was secretary of the Georgia Medical Society of Savannah from 1930, and served as its president in 1941. He was a member of the American Medical Association and Southern Medical Association, the American Roentgen Ray Society, the Radiological Society of North America, and a Fellow of the American College of Radiology. He was a member of the Georgia Radiological Society, serving as its president in 1948.

He was a civic minded man, and was president of the Chatham-Savannah Tuberculosis Association and a member of its board since 1932. It is of interest that this association was founded by Dr. McGee's mother in 1918. At the time of his death he was president of the Chatham County Health Council. He was a member of the First Bapist Church of Savannah, of Delta Kappa Epsilon and Phi Rho Sigma. He was a member of the Hibernian Society of Savannah, the Sons of the Revolution, the American Legion, Savannah Yacht and Country Club, and Savannah Golf Club, and for some time was a member of the Rotary Club of Savannah.

During World War II he served in the Medical Corps of the United States Navy from 1941 to 1945. He was transferred from active duty to the Reserves with the rank of Commander.

Dr. McGee is survived by his widow, Mrs. Helen Graham McGee; a son, Dr. Harry Hand McGee, Jr.; a daughter, Mrs. Marianna McGee Whalley; and a sister, Mrs. Theresa McGee Crenshaw.

Dr. McGee was an honor to his profession, he was regarded with high appreciation by his friends, and was a good citizen.

Robert Drane, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 29–Oct. 2, 1953.

American Radium Society
Secretary, Dr. J. E. Wirth, 635 Herkimer St., Pasadena 1, Calif. Annual meeting: Chase Hotel, St. Louis, Mo., April 20–22, 1953.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Palmer House, Chicago, Ill., Dec. 13–18, 1953.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: New York, New York, June 1–5, 1953.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 15 E. Monroe, Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
President, Dr. W. P. Stampfli, St. Luke's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. J. C. Cook, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. A. Judson Graves, 2002 Park St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. E. H. Bryson, 273 Alhambra Circle, Coral Gables, Fla. Meets third Wednesday of each month at Veterans Administration Building.

Houston Radiological Society
Secretary, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. James McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. Willis L. Beeler, M.D., 700 Kansas Ave., Topeka, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430 48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Joseph F. Linsman, 436 N. Roxbury Dr., Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Hugh Allan Smith, Eastern Maine General Hospital, Bangor, Maine. Meets in early spring, June and fall.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Will meet at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph J. La Vine, 259 North Grand Ave., Baldwin, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. R. Freid, 1049 Park Ave., New York 28, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. John F. Roach, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April. Annual meeting will be held in May or June, 1953.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. Richard C. Ripple, 1215 28th Street, Sacramento, Calif. Meets at dinner last Monday of September, November, January, March and May.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Willis S. Peck, 1838 Parkwood Ave., Toledo 2, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. J. Richard Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport. Annual meeting, Necho Allen Hotel, Pottsville, Pa., May 22 and 23, 1953.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. George P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. U. V. Wilcox, 915 Nineteenth St., N. W., Washington 6, D. C. Meets Medical Society Library, third Thursday of January, March, May and October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Harry K. Hines, 2508 Auburn Ave., Cincinnati 19, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Colonel Alexander O. Haff, M.C., Tripler Army Hospital, Honolulu, T. H. Meets third Friday of each month at Tripler Army Hospital.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Nicholas G. Demy, 912 Park Avenue, Plainfield, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. A. Gordon Ide, 277 Alexander St., Rochester 7, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Next annual meeting, Shirley-Savoy Hotel, Denver, Colo., August 20, 21 and 22, 1953.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

SAN DIEGO RADIOLOGICAL SOCIETY
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

Section on Radiology, California Medical Association
Secretary, Dr. Calvin L. Stewart, 2330 First Ave., San Diego 1, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Bay Radiological Society
Secretary, Dr. W. H. Graham, 634 East Santa Clara St., San Jose 12, Calif. Meets second Wednesday each month.

South Carolina Radiological Society
Secretary, Dr. Henry E. Plenge, Spartanburg General Hospital, Spartanburg, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, Newell Hospital, Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort worth 4, Texas. Next meeting, Dallas, Texas, Jan. 29 and 30, 1954.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

Westchester Radiological Society
Secretary, Dr. Clifford C. Baker, Harwood Bldg., Scarsdale, N. Y. Meets on third Tuesdays of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro Sede, Cordoba
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6º piso, Bogota, Colombia. Meets last Thursday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

SOCIÉTÉ FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALE, and its branches: SOCIÉTÉ DU SUD-OUEST, DU LITTORAL MÉDITERRANÉEN, DU CENTRE ET DU LYONNAIS, DE L'OUEST, DE L'EST, ET D'ALGER ET D'AFRIQUE DU NORD
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX^{e}, France.

CESKOSLOVENSK SPOLEČNOST PRO RËNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

WROCŁAW SECTION POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

DEUTSCHE ROENTGEN-GESELLSCHAFT
Secretary, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

INDIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

DR. CHARLES L. MARTIN HONORED

On the evening of March 16, 1953, during a meeting of the Dallas Southern Clinical Society, the local medical honor, the sixth annual Marchman Award, was given to Dr. Charles L. Martin of Dallas, Texas, for "outstanding scientific contributions and distinguished service to medicine." It was presented to Dr. Martin on the basis of his work in radiology over the last five years. His activities in this particular field over the years are well known to all radiologists. In 1940 Dr. Martin, with his father, another noted radiologist, the late Dr. James M. Martin, established a new clinic known as the Martin X-Ray and Radium Clinic adjoining Gaston Hospital, and in 1943 be became professor of radiology at Southwestern Medical College, successor to Baylor Medical College in Dallas. Dr. Martin is President of the American Roentgen Ray society, and past President of the American Radium Society, and he has held several other national professional offices. He has contributed numerous outstanding scientific articles to the medical literature and he has been a guest speaker at many medical conventions and cancer conferences.

ANNOUNCEMENT OF MEETINGS IN HOUSTON, TEXAS

Several meetings of interest to scientists and physicians will be held at the Texas Medical Center, Houston, Texas, on May 15 and 16.

These will include the *Seventh Annual Symposium on Fundamental Cancer Research* of The University of Texas M.D. Anderson Hospital for Cancer Research. One half day will be devoted to selected papers on the subject of "New Methods for the Study of Cells." *The Cancer Pathology and Radiology Conference* of The University of Texas M.D. Anderson Hospital and Postgraduate School of Medicine will be on "Tumors of Lung and Pleura." A meeting of the *South Central Section* of the *College of American Pathologists* will co-participate in the Symposium and Pathology Conference. There will be papers of general interest to pathologists. Dr. Robert C. Mellors, Department of Cytochemistry, Department of Experimental Pathology, Sloan-Kettering Institute, Memorial Hospital, New York, is arranging the session on cytological studies. Dr. David A. Wood, Professor of Oncology (Pathology) and Director of the Cancer Research Institute of the University of California School of Medicine, and Dr. W. Edward Chamberlain, Professor of Radiology, Temple University Hospital, Philadelphia, will conduct the pathology and radiology conference.

The fourth Bertner Foundation Lecture will be given by Dr. Charles C. Huggins, Professor of Surgery, University of Chicago School of Medicine, at the banquet on May 15; his subject will be "The Control of Human Cancer by Hormonal Methods." All meetings will be held at The Shamrock. Further information may be obtained from William O. Russell, M.D., at 2310 Baldwin Street, Houston 6, Texas.

CANADIAN ASSOCIATION OF RADIOLOGISTS

At a recent meeting of the Canadian Association of Radiologists the following officers were elected for 1953: *President*, Dr. R. A. Macpherson, Winnipeg, Manitoba; *Vice-President*, Dr. J. W. McKay, Montreal, Quebec; *Honorary Secretary-Treasurer*, Dr. D. L. McRae, Montreal, Quebec; *Associate Honorary Secretary-Treasurer*, Dr. Guillaume Gill, Montreal, Quebec.

NEW YORK ROENTGEN SOCIETY

The following have been elected the officers of the New York Roentgen Society for the year 1953–1954: *President*, Dr. Irving Schwartz; *Vice-President*, Dr. Harold W. Jacox; *Secretary*, Dr. Jacob R. Freid; *Treasurer*, Dr. Sidney Rubenfeld.

CORRECTION

The following corrections should be made in the article entitled "Photofluorography' for the Detection of Unsuspected Gastric Neoplasms" by Russell Wigh and Paul C. Swenson, published in the February, 1953, issue of the JOURNAL.

In the first column, third paragraph, page 242, the second sentence reads: "About 24,000 persons die of gastric cancer each year . . . . " This should be corrected to read: "About 42,000 persons die of gastric cancer each year . . . . "

In the discussion of the paper, the second column, next to the last paragraph, page 267, the last sentence in the paragraph reads: "I cannot give you Dr. State's figures today, but I do know that for the 14 asymptomatic persons the survival times exceed that which would be anticipated for asymptomatic cases." This should be corrected to read: " . . . exceed that which would be anticipated for symptomatic cases."

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

O'Rahilly, Ronan. Anomalous occipital apertures. *A.M.A. Arch. Path.*, June, 1952, *53*, 509–519.

Anomalous apertures of the occipital bone are not encountered frequently. A ten year old boy was examined because of a lump on the back of his head which had been noticed since birth. The lump was thought to be getting larger. The swelling was painful when touched. There was a cystic prominence over the occipital bone in the posterior median line. Compression of the neck caused an increase of pressure in the swelling.

Roentgenographic examination showed thinning of the occipital bone in its upper part and a circular bony defect was present in the median plane below the protuberance. A minute cleft-like extension proceded upward from the opening and was also median in location.

A case of occipital meningocele is illustrated. The patient was a boy who had a median cranial defect below the inion.

A review of the literature on occipital meningo-(encephalo-) celes and dermoid cysts shows that the associated cranial defects occur (a) rarely above the occipital protuberances (even as high as the lambda), (b) sometimes at the protuberances, or (c) most commonly between the protuberances and the foramen magnum. The defect may extend into the foramen magnum and may be associated with cervical spina bifida. A case of occipital opening associated with craniolacunia is mentioned, and the association between meningocele in general and craniolacunia is noted.

Defective occiput and bifid vertebral arches are both median deficiencies in the dorsal wall of the neural axis. Recent writers on craniospinal defects stress the influence of cerebrospinal fluid disturbances, but some authors concede other modes of formation, also.

Opening near the apex of the occipital bone (which is believed by Boyd to "correspond" with the human parietal foramen) is sometimes encountered in primate skulls, and a well marked case is illustrated. There is no evidence available that anomalous occipital apertures are related to any of these normal openings.

The development of the human occipital bone (from basioccipital, exoccipital, and supraoccipital, and interparietal portions) is summarized. The relevant embryology suggests that anomalous median occipital apertures are located (a) between the interparietals, (b) at the interparietal-supraoccipital junction, or (c) most commonly in the region of the "occipital fissure." If it is held that pressure effects are of importance in the formation of cranial defects, then the "occipital fissure" may be regarded as a site of decreased resistance. The basis of such features as the localization of the defect remains entirely unknown.—*Robert K. Arbuckle, M.D.*

Netsky, Martin G., and Strobos, R. R. J. Neoplasms within the midbrain. *A.M.A. Arch. Neurol. & Psychiat.*, July, 1952, *68*, 116–129.

The authors add 4 cases of their own to the 19 neoplasms of the midbrain already described in the literature.

The cases were difficult to diagnose because of few localizing signs. Prominent mental changes preceded the signs and were misleading.

Air studies were helpful. Usually there was a symmetrical dilatation of the lateral and third ventricles, with impingement on the posterior aspect and floor of the third ventricle. Enlargement of the fourth ventricle with a block of the aqueduct was described in 1 case and was considered to be unusual.

Air studies were followed by death in 2 cases.—*Lawrence A. Davis, M.D.*

Drewes, H. G. Die Lageänderung der verkalkten Zirbeldrüse auf dem Röntgenbild bei gerichteter intrakranieller Schrumpfung nach offenen Gehirnverletzungen. (Displacement of the calcified pineal gland in intracranial atrophy after open cerebral trauma.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1952, *77*, 77–80.

Calcified pineal glands were seen in 80 per cent of mostly male adults, while the literature gives percentages of from 55 to 75. Much has been published about displacement of it by space occupying lesions.

The author examined 258 roentgenograms of skulls with calcified pineal glands after cerebral injuries with bone defects of the skull, the size of which was at least that of a hazelnut, usually larger. These defects were either due to the injury itself or to the surgery following the injury.

By shrinkage of the cerebrum caused by the scar, a displacement of those parts of the brain which neighbor the injured area takes place in the direction of the defect in the skull. Because of the localized brain atrophy there is often a localized dilatation of the neighboring ventricle and often a displacement of the pineal gland.

When there was a skull defect in the parietal bones, displacement of the calcified pineal gland was present in 38.9 per cent, always in the direction of the defect. In the frontal area the percentage was 43.6 per cent; in the occipital region 25 per cent and in the temporal area 27.3 per cent.—*Hans W. Hefke, M.D.*

Ghersi, Julio A. Angiografía cerebral; algunos aportes técnicos. (Cerebral angiography;

some technical considerations.) *Prensa méd. argent.*, Aug. 18, 1950, *37*, 1933–1934.

Cerebral angiography was introduced by the Portuguese neurosurgeon Egas Moniz, this being one of the reasons why last year he received the Nobel Prize in Medicine. Through the years various difficulties have been overcome and a perfected technique arrived at, including injection of the arterial system by the open or closed method, the development of less a toxic and more radiopaque substance, and the invention of apparatus for making the serial roentgenograms which provide the maximum of information. The author submits additional improvements in the technique. Once the carotid or cerebral artery has been entered, it is important to allow a certain time to elapse between the moment of injection and the taking of the roentgenograms in order to coordinate the other details of the examination. There are also a number of precautions to be observed: the lumen of the needle should not be obstructed by coagulum, lest small coagula should be impelled into the circulatory stream. Means have been discovered for keeping the needle open in case it is necessary to repeat the injection.

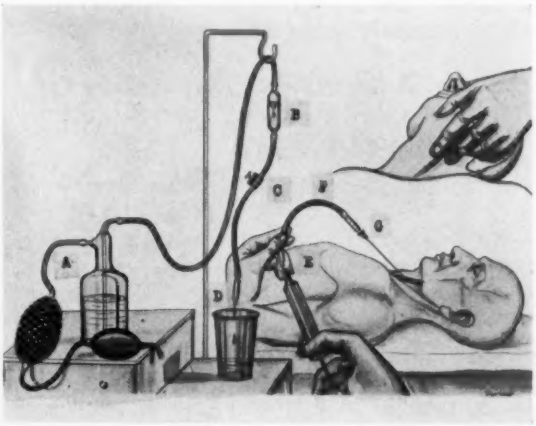

Fig. 1. Schematic illustration of the system of injection in cerebral angiography. (*A*) Serum bottle with a Richardson bulb which permits the establishment of a sufficient pressure to obtain in (*B*) a continuous drip through the controlled resistance of interrupter (*C*) into the artery. The intermediary tube (*F*) is made of resistant plastic material and has a lumen 3 mm. in diameter. The arterial puncture is performed by the open or closed method with the aid of a needle provided with a mandrel. After the artery is entered the mandrel is withdrawn and the needle is connected with the intermediary tube at (*G*). The drawing shows the phase when the tubing system is disconnected at *D-E* for the injection of the contrast medium after which the connection is re-established and further serum is allowed to flow into the artery. In the right upper background the percutaneous puncture of the common carotid artery is illustrated. (Reproduced by permission from *Prensa méd. argent.*, 1950, *37*, 1933–1934.)

Lisson devised a scheme for injecting artificial serum with an ordinary syringe to keep the needle open, attaching the needle by the intermediary of a rubber tube. This degree of manipulation requires a change of solution when the content of the syringe in use has been emptied. This brings about a number of small difficulties, one of them, for example, being the reflux of blood each time the change is made, a happening which may obstruct the needle by coagula, if indeed they do not encourage small emboli.

This is why the author devised the procedure of continuous injection of artificial serum to give time for the adaptation of the other necessary elements to obtain the roentgenograms. In the accompanying illustration (Fig. 1) the author shows the technique schematically and describes some of the details. It is a system in which the solution is under pressure. The secret is to utilize strong tubes which do not inflate, attached with strong ligatures to make sure that the connections do not loosen. Special attention is given to the segments which connect the syringe and the needle during the injection of the contrast substance. None of these elements for the examination should be used without having tested the ligatures and the intermediary tubes. Another of the tricks is to remove absolutely all the air from the tube. This is no more difficult than with the apparatus for blood transfusion. It is important to have liquid flowing at the moment of making connections. In this way penetration of air into the tube will be avoided. —*James T. Case, M.D.*

Younghusband, Omar Z., Horrax, Gilbert, Hurxthal, Lewis M., Hare, Hugh F., and Poppen, James L. Chromophobe pituitary tumors. 1. Diagnosis. *J. Clin. Endocrinol. & Metabol.*, June, 1952, *12*, 611–630.

The authors review 164 presumed cases of chromophobe pituitary adenomas. The diagnosis was verified histopathologically in 105 patients. The remaining 59 patients were diagnosed on the basis of roentgen findings in association either with primary optic atrophy and bitemporal visual field defects or with evidence of pituitary dysfunction.

The presumptive diagnosis of chromophobe tumor is usually justified in the presence of an enlarged sella, well marked signs of hypopituitarism, and primary optic atrophy together with bitemporal visual field defects.

Adenomas usually begin as small discrete tumors which grow slowly. The normal pituitary gland occupies about 50 per cent of the volume of the sella turcica, hence at first there is room for the adenoma to grow. As the adenoma grows, the normal pituitary

is compressed and finally the adenoma breaks through the boundaries. It can extend then in various ways causing different symptoms. In most cases the classic visual defect, bitemporal hemianopsia, occurs as the tumor impinges on the optic chiasm. The visual field defects usually begin as scotomas or cutting-in of the superotemporal quadrants. A progressive defect in the visual fields is an important criterion in the diagnosis. Relief of pressure on the optic nerve usually results in visual improvement, but vision may be permanently damaged if the adenoma compresses the nerves against the laterally placed carotid artery.

Chromophobe tumors are usually benign, but a certain number of them recur after surgical removal. Many of the adenomas are cystic, of one of two types: (1) the commoner hemorrhagic type, due to hemorrhage into degenerated areas of adenomas, and (2) cysts which contain xanthochromic fluid formed by chromophobe cells. Most adenomas begin in middle adult life. Both sexes are affected about equally.

Symptoms are caused by pressure or extension of the tumor into adjoining neural structures or by the clinical picture arising from the hormonal insufficiencies caused by the tumor pressing on or destroying the remaining functioning pituitary tissue, or the hypothalamus, or both.

The symptoms from pressure presented in this series of patients were first of all visual disturbances found in 80 per cent, secondly, headache present in 66.8 per cent and finally, neurologic manifestations of a nonspecific variety such as stupor, coma, personality changes and a variety of symptoms similar to those produced by cerebral pressure from any cause.

Clinically endocrine deficiency occurs following pressure upon or destruction of functioning pituitary tissue. Underfunction is manifested by secondary depression of the function of the peripheral endocrine glands, especially the thyroid, adrenals, and gonads. Histories of patients are presented illustrating how chromophobe tumors can simulate Addison's disease and myxedema. Histories are also presented in which the chief complaints were amenorrhea, loss of libido, sterility, anemia and fatigue.

The physical findings occur mainly in the skin, sexual hair, genitalia and fund . The skin is usually soft and smooth, sexual hair is characteristically reduced or absent. The testes are often small and soft. Osteoarthritis is usually rare. The blood pressure is often low. The optic fundi usually reveal primary atrophy of the optic nerve. The visual acuity is most often impaired. The blood findings are those of a normocytic anemia due to a hormonal deficiency especially that of the secondary hypoadrenocorticism.

The basal metabolic rate averages minus 20 per cent. Plasma cholesterol is slightly above normal. Blood sugar is normal. Hormonal studies are not too revealing.

Roentgenographic features are those of a distorted or enlarged sella turcica associated with ballooning, thinning and depression of the floor, either bilaterally or unilaterally. A review of 1,000 roentgenograms of the skull revealed the arbitrary upper limits of the sella area in the adult at 140 sq. mm. In the authors' series only 2 patients had normal sized sellae and in these 2 patients thinning or evidence of ballooning was present. Exploration because of clinical changes revealed large extrasellar chromophobe tumors. The measurements in this series were mainly under 300 sq. mm., although several instances of larger sellae, ranging up to 468 sq. mm. were noted.

Thinning or absence of the posterior clinoid processes with posterior displacement and depression or breaking through of the floor into the sphenoidal sinus was frequently noted. Rarely, flecks of calcium may be observed in or above the sella. Reduction in size of the sella after treatment is unusual. In only a few cases was a calcified pineal body displaced.

Differential diagnosis from an aneurysm of the internal carotid artery can be made by the presence of calcium, absence of visual defects, and by angiography.—*Frank J. Rigos, M.D.*

HORRAX, GILBERT, HARE, HUGH F., POPPEN, JAMES L., HURXTHAL, LEWIS M., and YOUNGHUSBAND, OMAR Z. Chromophobe pituitary tumors. II. Treatment. *J. Clin. Endocrinol. & Metabol.*, June, 1952, *12*, 631–641.

The primary object of treatment of chromophobe pituitary tumor or its complications is the arrest or restoration of visual loss. Treatment consists of roentgen irradiation, surgery or a combination of the two and the administration of natural or synthetic hormonal substances when secondary glandular deficiencies exist.

Roentgen irradiation has been given before considering surgery when the reduction in vision has not been marked or when visual loss has not been rapid. The dosage of radiation now used is a tumor dosage of 4,000 roentgens given by the rotational technique. In this series of patients, however, 1,800 r tumor dose was given through two lateral 5 cm. temporal portals.

Improvement following irradiation may be prompt or gradual. Hemorrhage into the adenoma during roentgen therapy causes increased pressure on the optic nerves and causes rapid visual loss. This is an indication for immediate surgery. Progressive deterioration of vision or scintillating scotoma are other indications for surgery.

Surgery has been performed by the intradural transfrontal approach. The indications for surgery are: (1) marked visual impairment; (2) recent rapid visual loss; (3) progressive visual impairment despite adequate roentgen treatment; (4) visual impairment arrested at an incapacitating level, despite irradiation; (5) large tumors with extrasellar extension

causing central nervous system symptoms; and (6) a clinical picture not altogether typical of a pituitary tumor and compatible with another type of chiasmal lesion.

One hundred and five patients were operated on, 36 patients had had previous roentgen treatment which failed. The over-all surgical mortality was 14.1 per cent for all types of growth with or without intracranial extension. Hyperthermia after operation is often the cause of death. At present ACTH is given immediately after surgery and this would appear to prevent or reduce hyperthermia. Seventy-two per cent of the patients operated on five or more years ago survived for from five to eighteen years. Seventy-seven per cent had improved vision for six years following surgery. Surgery combined with irradiation was used in 60 patients with improvement in vision in 68 per cent. Surgery after failure of irradiation in 36 patients gave improved vision in about 60 per cent. Roentgen treatment in 50 patients gave visual improvement in 59.3 per cent.

When clinical evidence of pituitary deficiency was present desoxycorticosterone along with testosterone was used followed by the addition of desiccated thyroid in a month or two.

During the past two years ACTH has been used with good results as concerns greater endurance and a feeling of well-being. Testosterone and desoxycorticosterone are given since the daily requirement of ACTH may be lessened. Cortisone may be used instead of ACTH.

Thyroid medication helps those patients with clinical evidence of myxedema. Desoxycorticosterone causes an increase in blood pressure and a sense of well-being. Testosterone causes nitrogen retention, synthesis of protein, regrowth of hair, lessens fatigue and restores libido. Desoxycorticosterone does not always have to be maintained since the blood pressure may remain elevated long after the pellets are exhausted.

Improvement in the red blood cell count and hemoglobin does not occur readily despite treatment. —*Frank J. Rigos, M.D.*

Land, Richard N. Glomus jugularis tumor of the middle ear; a case report. *Radiology*, July, 1952, *59*, 70–76.

Glomus jugularis tumors are carotid body-like tumors usually found in the adventitia of the dome of the jugular bulb, immediately below the bony floor of the middle ear and near the ramus tympanicus of the glossopharyngeal nerve. They give rise to such findings as deafness, headaches, facial paralysis, dizziness, discharge from the ear, and soft dark purplish masses in the external ear.

Roentgenologically, one sees extensive bone destruction in the mastoid process and petrous portion of the temporal bone, as the result of pressure necrosis, and extension.

To be considered in the differential diagnosis are benign tumors, fibrous dysplasia, other malignant tumors and especially cholesteatomas. Cholesteatomas are usually slow-growing and a protective zone of calcification forms about the periphery, so they are characterized by a sharply marginated area of rarefaction.

A case of this unusual tumor of the middle ear is reported.—*McClure Wilson, M.D.*

Stafne, Edward C. Dental roentgenologic manifestations of systemic disease. III. Granulomatous disease, Paget's disease, acrosclerosis and others. *Radiology*, June, 1952, *58*, 820–829.

This is the third and last of Stafne's series of articles on the manifestation of systemic disease in the dental roentgenogram.

Syphilis. Syphilis may be detected early by study of the shape of the teeth and their size. The screw driver-shaped crown and notched incisal edge of central incisors as described by Hutchinson and the "mulberry molars" may occur in congenital syphilis. Since the crowns of these frequently form by one year of age, the roentgenogram may be of help in differential diagnosis at this early age.

Hand-Schüller-Christian Disease. This disease is a disturbance of the reticuloendothelial system, most often occurring in early life. Diabetes insipidus and exopthalmos are frequently associated with bone defects, which occur most often in the calvarium, jaws, scapulae, pelvis and ribs. The bone defects are produced by granuloma-like accumulations of connective tissue which may contain a large number of foam cells loaded with fat. In the jaws of children, the granulomatous tissue has a predilection for forming in the periapical region or dentin papilla of teeth which are undergoing development. With the expansion of the lesions, the alveolar socket or the dental crypt, depending which, is destroyed and the partially developed teeth are forced from their original position and exfoliated. In the roentgenogram the exfoliating teeth have the appearance of floating in space, which is distinctive and diagnostic of the disease. Roentgen therapy for the early jaw lesions may be a means of preventing extensive loss of teeth, since such therapy has destroyed the other bone lesions.

Eosinophilic Granuloma of Bone. An eosinophilic granuloma is a destructive lesion of bone consisting of granulomatous tissue. It may be solitary or multiple, and consist of large accumulations of histiocytes with a variable number of eosinophilic leukocytes. There appears to be no systemic reaction to the disease, and the lesions respond readily to curettage and roentgen therapy. The incidence in jaws is about 5.5 per cent, which is less than in Hand-Schüller-Christian disease. The roentgen appearance varies. A solitary lesion may occur in the medullary

portion as an oval or round area of rarefaction which may have fairly sharply outlined margins or erosion of the cortex of the alveolar bone may take place, subsequently sloughing the teeth from the area.

Multiple Myeloma. This is characterized by multiple neoplasms formed from bone marrow cells of the plasma cell series. These neoplasms may be widely scattered throughout the skeleton particularly in the ribs, sternum, skull, clavicles and spinal column. The roentgen appearance of the early stage is that of small radiolucent areas confined to bone marrow. These coalesce with development and form irregularly defined areas of radiolucence. The cortex is secondarily involved by direct extension and invasion, which occasionally entirely destroy the bone.

In the jaws there may be a spotty distribution of lesions throughout both maxilla and mandible, but usually only the mandible is affected. Here the initial lesions tend to appear in the posterior regions, where the marrow spaces are largest, extending forward along and below the mandibular canal. There is also a tendency to extension up into the marrow spaces of edentulous regions. The roentgen appearance of the process in the jaws is variable, and is not diagnostic of the disease.

Paget's Disease (*Osteitis Deformans*). Paget's disease is a skeletal disease usually occurring after middle life. One or more bones may be involved, and the primary lesion may occur in the maxilla or mandible. The jaw incidence is relatively high, the maxilla being affected most often, and rarely both maxilla and mandible. The stage of the disease determines the roentgenographic appearance. In the early or resorptive stage, the lesion produces a radiolucent area with alteration of the trabecular pattern into one which has a fine lace-like resemblance. This radiolucency is more marked in the periapical regions, and often presents the appearance of pseudocysts on the roots of the teeth. There is disappearance of the lamina dura in the involved regions and at this time there may also be evidence of variable amounts of resorption of the roots of some of the teeth. This stage is probably comparable to the stage of osteoporosis circumscripta of the skull which is associated with Paget's disease.

In the advanced stage, when an excessive amount of dense sclerotic bone appears, the roentgenogram reveals alternating areas of osteoporosis and osteosclerosis, due to the differences in the ratio of osteoblastic and osteoclastic activity. With increased osteoblastic activity, there is also deposition of poorly differentiated cementum on the roots of some of the teeth. This excess of hyperplastic cementum is peculiar to Paget's disease, and is used as a differential point in other osseous disease.

Acrosclerosis. Acrosclerosis, a variety of scleroderma, chiefly involves the fingers, shoulder girdle, face and sometimes the mucous membranes of the oral cavity. There is also, in approximately 10 per cent of cases, an abnormal increase in the width of the periodontal membrane space, which presents a dental roentgenographic picture that is apparently peculiar to patients with acrosclerosis and scleroderma. The enlarged space tends to surround the entire root of the tooth and is almost uniform in width. Microscopically there is a notable increase in the size and number of collagenous fibers. There is also thickening of the walls of the vessels. There is roentgenographic evidence of resorption and destruction of the wall of the socket, later followed by sclerotic changes in the wall. This is evidenced by a wide radiopaque line which eventually outlines the limits of the enlarged socket. The teeth remain firm.

Rickets. Vitamin D function is to maintain the level of calcium and phosphorus in the blood in normal amounts and in a normal ratio. Deficiency of vitamin D affects primarily the growing skeleton. Osteoid tissue fails to undergo proper calcification and the bones remain soft and are prone to bend. Infantile rickets, which has its greatest incidence between three months and three years of age, often causes mental disturbances. The most common of these is hypoplasia of the enamel. Others are retarded development and eruption of the teeth and malocclusion.

In late rickets (rachitis tarda), which occurs at about six years of age or later, the dental disturbance is less severe. Hypoplasia of the enamel may be absent, but retarded development of the roots and malocclusion may be present to a varied degree.

Osteomalacia. This is an adult disease, which may be due to an excessive excretion of calcium from the body or to deficient absorption of calcium from the intestinal tract. There is defective calcification in the bone matrix, which may result in bones consisting predominantly of osteoid tissue. Roentgenographically there is a uniform, generalized appearance of decalcification, often with an unusual absence of trabecular structure. The cortex of the bones is thin, and there is lack of subperiosteal resorption. Since the disease onset occurs after termination of skeletal growth, the teeth are not affected; their osseous support undergoes changes similar to those which occur in other bones.

Hematogenous Osteitis. Hematogenous osteitis is a metastatic infection which produces the typical symptoms of osteomyelitis. It is most often caused by *Staphylococcus aureus.* It occurs most frequently in children and adolescents, following injuries, skin infections, measles, scarlet fever, and other childhood diseases. Several bones may be involved successively or simultaneously.

Radium Osteosis. Radioactive substances when taken by mouth may remain permanently in bone and emit radiations which, among other things, produce osteosis and severe leukopenic anemia. Resistance to infection in the bone is lowered and osteomyelitis of the jaws, an outstanding feature, occurs as a result of superadded bacterial infection from periodontal and periapical disease, which is com-

monly present. When acute and active osteomyelitis occurs, the roentgen appearance may be very similar to that of osteomyelitis originating from other sources. There may be irregular areas of destruction of bone throughout both jaws, with evidence of condensing osteitis about some of these areas suggesting an inflammatory process. The history (occupational) and study of other bones may furnish valuable information.—*Dean Nichols, M.D.*

Dechaume, M., Bonneau, M., and Payen, J. La lithiase sous-maxillaire (réflexions suggérées par 60 observations). (Submaxillary stones; considerations suggested by 60 observations.) *Presse méd.*, June 18, 1952, *60*, 908–910.

On the basis of 60 observations, the authors believe that according to their sialographic findings submaxillary salivary stones always occur in association with a dilated Wharton's duct. The whole duct was found dilated, not merely the segment at the level of the stone. Reflex disturbances may cause contraction of the circular fibers of the duct, produce blockage with secondary infection and induce formation of stones.

The authors never found fungi in these stones, contrary to the report by Soderlund.

The stones were multiple in 15 of the 60 cases. All the stones were in Wharton's duct, none were seen in the gland itself.

The authors used iodized oil for sialography, preceded by plain roentgenograms of the submandibular area.

The clinical manifestations did not seem to correspond to the size of the stone or stones.

The article contains many interesting roentgenographic reproductions and a fairly detailed description of the technique which the authors are using.—*Albert Oppenheimer, M.D.*

Neck and Chest

Orban, F., and Foret, J. Diagnostic et traitement des perforations oesophagiennes récentes. (Diagnosis and treatment of recent esophageal perforations.) *Acta gastro-enterol. belg.*, June, 1952, *15*, 526–536.

The basis of this report is formed by 2 cases of endoscopic perforation of the esophagus, which is the cause of about 65 per cent of secondary esophageal perforations (dilatations are included in this estimate). Diagnosis should not be difficult.

Often the endoscopist notes a little hemorrhage or meets resistance. The exploration may have been a tedious procedure. Pain at the moment of perforation may not be violent; it may not reach a maximum for several hours. The pain depends on the location and method of perforation. There is a rapid appearance of shock. Dysphagia and fever appear early. Signs of mediastinitis with or without pleural involvement appear later, in two to four hours.

Roentgenographic examination is of variable use. When a foreign body is present and is opaque, diagnosis and localization are prompt. After several hours, there may be gas in the tissues of the neck, gas or fluid in a widened mediastinum, eventually a compressed trachea, pleurisy with or without pneumothorax, pneumopericardium.

Opacification of the esophagus should be done with lipiodol, not barium. With small perforations, however, the fistula may not be demonstrated.

All cases of perforated esophagus should be operated upon promptly. The aim is to drain and limit mediastinal cellulitis, to drain the pleura if involved and suture the perforation. Gastrostomy or jejunostomy may be indicated. Massive antibiotic therapy should be administered.

Prognosis is in proportion to the adequacy of treatment. The mortality should be less than 50 per cent, and in the best circumstances, less than 20 per cent. —*Marcy L. Sussman, M.D.*

Heinbecker, Peter. Recent advances in our knowledge of the thyroid gland. *Ann. Surg.*, July, 1952, *136*, 145–161.

A discussion of the physiology of the thyroid hormone, the relationship of the thyroid to other endocrine glands, and of the pathogenesis of hyperthyroidism is given. Attempts to prove the possible relation between parathyroid and thyroid glands have been made. Experimental evidence seems to suggest that the hypophyseal basophilic cells are tropic to the thyroid gland but inhibitory to the parathyroid glands.

The role of iodine, the choice of antithyroid substances and the recent development of radioactive iodine in the treatment of hyperthyroidism are briefly reviewed.

Surgery as a form of therapy for diseases of the thyroid gland still has a wider applicability than other forms now available. For Graves' disease treatment with radioactive iodine promises to be as effective as surgery.—*C. C. Wang, M.D.*

Wise, Burton L., and Hart, Joseph C. Idiopathic hypoparathyroidism and pseudohypoparathyroidism; observations on the electroencephalogram in hypocalcemia. *A.M.A. Arch. Neurol. & Psychiat.*, July, 1952, *68*, 78–93.

In the American literature 34 cases of idiopathic hypoparathyroidism have been recorded up to February, 1945. The authors report 2 cases of this condition as well as 1 case of the even more rare pseudohypoparathyroidism. All 3 cases were seen in King's County Hospital during the years 1948 and 1949.

The 2 cases fulfilled the criteria for diagnosis of

idiopathic hypoparathyroidism, *i.e.*, low serum calcium, elevated serum phosphorus, normal serum alkaline phosphatase and absence of roentgenographic signs of active rickets or osteomalacia and the absence of renal insufficiency.

The third case, in which abnormalities of serum calcium and serum phosphorus were also present, was diagnosed as pseudohypothyroidism principally on the basis of the failure of phosphate diuresis to occur following intravenous administration of parathyroid extract (Ellsworth-Howard test). Physical features, said to be characteristic of pseudohypoparathyroidism, are described. This patient had bilateral cerebral calcification in the region of the basal ganglia, which has been reported as characteristic of chronic hypocalcemic states.

Two of the patients described had had convulsive seizures and had abnormal electroencephalograms, which are described. Following therapy and return of serum calcium to normal levels, the electroencephalograms improved remarkably but continued to show minimal abnormalities. Anticonvulsive drugs were unnecessary in these 2 cases.—*Doris E. Pipkin, M.D.*

FISHER, EDWIN R., COBURN, DONALD, and EFFLER, DONALD B. Thymic neoplasms. *J. Thoracic Surg.*, July, 1952, *24*, 58–69.

The literature pertaining to thymic neoplasms is reviewed, with an attempt toward presenting a simplified understanding of terminology, embryology and classification of these neoplasms.

Thymic tumors may be classified into: (1) lymphosarcoma; (2) carcinoma; (3) lymphoepithelioma, and (4) carcinoma, granulomatous type.

Five cases of thymic tumor are reported, 2 of which had an associated myasthenia gravis.

The frequent occurrence of invasion of adjacent structures, as well as the occurrence of distant metastases and lack of histopathologic difference between so-called benign and malignant thymic neoplasms, indicates that all such tumors must be regarded with suspicion. The recurrence of a tumor, which had been apparently encapsulated and completely removed, two years after operation emphasizes the caution necessary in prognosticating the clinical behavior of these neoplasms.

There is no histopathologic criterion by which the thymic tumors associated with myasthenia gravis can be differentiated from those unaccompanied by this disease.

Thymic tumors unassociated with myasthenia gravis may be asymptomatic. Only 1 of the 3 patients without myasthenia gravis presented the more classical symptoms of thymic tumor.

It appears that surgical extirpation is the treatment of choice, although many cases on initial observation are inoperable. Nitrogen mustard therapy, or roentgen therapy, has been for the most part disappointing in the inoperable cases.—*Thomas C. Stansbury, M.D.*

MADOFF, IRVING M., GAENSLER, EDWARD A., and STRIEDER, JOHN W. Congenital absence of the right pulmonary artery; diagnosis by angiocardiography with cardiorespiratory studies. *New England J. Med.*, July 31, 1952, *247*, 149–157.

The first case of an absent major branch of the pulmonary artery was first recorded in 1868. Since that time a total of 9 cases have been reported, 7 of which were diagnosed at postmortem studies, and 2 at surgery. The authors present at this time a case of a fourteen year old girl who had an absent right pulmonary artery diagnosed by angiocardiography.

The 9 previously reported cases had had one or more associated anomalies of the heart or great vessels. In 6 of these cases the right pulmonary artery was absent, and in 3 the left.

Roentgen studies of the chest in the authors' case demonstrated a shift of the trachea to the right. The esophagus was in the midline with a small pressure defect on the left and anteriorly. A slight oblique defect was noted in the posteroanterior projection approximately 2.5 cm. below the sternal notch. The left lung appeared hyperventilated and the left side of the hemithorax was larger than the right. The upper portion of the left lung herniated across the midline. In this case the "hilar comma" was present.

Because a vascular anomaly was suspected, angiocardiographic studies were performed. At $4\frac{1}{2}$ seconds a normal left pulmonary circulation was demonstrated, but not until at eight seconds was the right pulmonary circulation visible. This was interpreted as indicating circulation to the right lung from anomalous branches arising near the arch of the aorta.

Pulmonary function studies showed only slight reduction in maximum breathing and vital capacities, residual volume and total lung capacity. Intrapulmonary mixing and arterial oxygen saturation were normal. The right lung without a normal pulmonary artery showed a normal ventilation but did not participate in oxygen uptake. It was estimated that 17 per cent of the systemic circulation entered the right lung.

The authors consider the therapeutic implications of such an anomaly and conclude that pneumonectomy might be necessary if hemoptysis results due to inability of the pulmonary vascular bed to withstand the high pressure of systemic circulation. Cardiac failure may result because a large anomalous artery may produce in effect an arteriovenous shunt. The main circulatory burden produced by this anomaly is the increased load placed upon the left ventricle, and there is very little effect upon the pressure in the right ventricle.—*Robert L. Raphael, M.D.*

BALLON, HARRY C. Superior vena caval obstruction. *Ann. Surg.*, July, 1952, *136*, 39–43.

The author reports a case of superior vena caval

obstruction due to calcified superior mediastinal masses of unknown etiology which has been followed for six years with little change. He suggests that the masses might represent calcified tuberculous lymph nodes or Hodgkin's disease but goes on to refer to Erganian and Wade who expressed doubt as to the validity of the concepts of tuberculous and syphilitic mediastinitis.

In the author's own experience, the two most common causes of venous hypertension due to superior vena caval obstruction are inoperable carcinoma of the lung and metastatic carcinoma of the breast.—*Martin B. Levene, M.D.*

Dammann, J. Francis, Jr., and Sell, C. Gordon R. Patent ductus arteriosus in the absence of a continuous murmur. *Circulation*, July, 1952, *6*, 110–124.

Diagnosis of patent ductus arteriosus is difficult when the classic continuous murmur is not present. In infancy, in the presence of cardiac decompensation and when the ductus approximates the aorta in size, a continuous murmur is frequently absent. The association of a large patent ductus approximating the size of the aorta with pulmonary hypertension, absence of a continuous murmur and great cardiac enlargement is striking. Long continued pulmonary hypertension may lead to irreversible changes in the pulmonary vascular bed. This affords strong argument for early closure of a large patent ductus arteriosus.

The authors present a review of 24 surgical patients in whom the clinical diagnosis of patent ductus was considered despite the absence of a typical continuous murmur. Of the 24 patients, 15 were proved to have large patent ductuses, 2 to have aortic septal defects and 7 to have high ventricular defects or hearts of the Eisenmenger type. Three representative examples are described in detail.

The clinical syndrome in all patients was remarkably uniform despite distinct differences in the malformation present. The findings were usually failure to grow and develop normally, repeated episodes of pneumonia, dyspnea, early onset of cardiac failure, a high pulse pressure and bounding pulse, splitting and accentuation of the second sound at the base, a systolic murmur along the left sternal border and commonly an apical rumbling mid-diastolic murmur.

Fluoroscopic examination and roentgenograms demonstrated generalized cardiac enlargement and usually specific enlargement of the left auricle. The pulmonary vascular markings were noted to be increased and often a hilar dance was present. Electrocardiography frequently showed a normal electric axis, and no ventricular hypertrophy in the precordial leads. In those patients catheterized, there was marked pulmonary or right ventricular hypertension. Angiocardiography was attempted in only one patient. Opacification of the descending aorta immediately after or simultaneously with the main pulmonary arteries suggested a shunt through a patent ductus from pulmonary artery to aorta. Retrograde aortography has been reported to be of value.

The authors stress the high percentage of diagnostic error in their series and the surgical mortality of 4 out of 24 patients, dying as result of operation. They insist, therefore, on better nonoperative diagnostic measures. In their series, catheterization and aortography proved most helpful. They believe that the latter may be of better aid in the future. Although complete follow-up studies are not available at this date, they note that most of the patients shown to have a patent ductus improved considerably.—*Alexander S. Macmillan, Jr., M.D.*

Tomlin, Clyde E., Logue, R. Bruce, and Hurst, J. Willis. Chronic cor pulmonale as a complication of fibrocystic disease of the pancreas. *Am. Heart J.*, July, 1952, *44*, 42–50.

In fibrocystic disease of the pancreas, obstruction of the bronchi by thick, tenacious, purulent sputum produces areas of hyperexpansion, atelectasis, and lobular pneumonia. As the disease progresses, bronchiectasis and pulmonary abscesses develop. Due to the extensive destruction and alteration of the pulmonary parenchyma, it has been estimated that chronic cor pulmonale will occur in 70 per cent of infants and children dying from fibrocystic disease. Until recently, however, few clinical observations have been made concerning this complication.

Cor pulmonale with right ventricular failure in combination with fibrocystic disease of the pancreas presents a problem in diagnosis. Cyanosis, if present, may be due to the widespread pulmonary pathology or to the cardiac failure, or to a combination of both. Hepatomegaly may be the result of right heart failure or fatty infiltration and/or cirrhosis of the liver, common in fibrocystic disease. The electrocardiogram is frequently of no help as it may show the normal right ventricular hypertrophy pattern of infancy or the vertical position of the heart in an emphysematous chest.

Roentgenograms of the chest made during life may reveal a cardiac configuration suggesting right ventricular enlargement, but most often the findings are not clear-cut.

Because of these diagnostic difficulties the authors believe that the diagnosis of right ventricular hypertrophy in association with cor pulmonale secondary to fibrocystic disease can only be diagnosed with certainty by postmortem study.

Two illustrative cases are discussed.—*Harold Fulton, M.D.*

Powers, L. E., and Lainhart, Wm. S. Errors of diagnosis in mass radiography. *Radiology*, July, 1952, *59*, 88–91.

A mass chest survey using 70 mm. photofluoro-

grams carried out at Tacoma, Washington, in 1949 yielded 506 patients with abnormal chest findings, who were adequately followed for two years in addition to having subsequent 14 by 17 inch roentgenograms. An additional 171 individuals with abnormal photofluorograms were either lost or excluded because of inadequate follow-up.

Dividing the abnormalities into four groups, namely, tuberculosis, suspected tuberculosis, cardiac, and others, it was found that the photofluorograms gave a reading error of 18.6 per cent as compared to a reading error of 16.2 per cent for the conventional roentgenograms.

On investigation of 254 new cases of tuberculosis reported during the two year follow-up period, it was found that only 2 had taken advantage of the survey and that both had positive photofluorograms.

Hence, if the 171 "lost" cases are not considered, it may be concluded that (1) the number of cases "missed" by present photofluorographic methods is insignificant, (2) many individuals may suspect that they have tuberculosis and avoid the examination, and (3) the error in interpretation from the two sizes of roentgenograms are not significantly different.—*Martin B. Goodwin, M.D.*

KANE, IRVING J., and HEISER, SAUL. Indications for a delayed roentgenogram in bronchography. *J. Thoracic Surg.*, July, 1952, *24*, 70–74.

In mapping out the extent of surgical resection for a patient with bronchiectasis, a delayed film following bronchography may prove to be of considerable value. Often important in establishing the presence of bronchiectasis, such a delayed film may also help avoid needless sacrifice of tissue by eliminating uncertainty concerning a specific bronchial segment. Lung tissue may thus be conserved without the risk of compromising a complete cure.

A delayed roentgenogram is indicated when examination of the wet film taken mmediately following bronchography discloses adequate contrast substance in a proximal bronchus, associated with failure to outline its peripheral branches. In the interval before taking such an additional roentgenogram, the patient should be maintained, for about five minutes, in a position favoring gravitation of the contrast substance into the unfilled segments. In the latter position he should be instructed to breathe very slowly and deeply, encouraging maximum dilatation and elongation of bronchi as a further aid to entrance of the iodized oil.

Bronchograms are presented from 3 representative cases.—*Thomas C. Stansbury, M.D.*

MANDEZ, FERNANDO L., JR., LEAHY, LEON J., and BUTSCH, WINFIELD L. Some aspects of bronchiectasis in infants. *J. Thoracic Surg.*, July, 1952, *24*, 50–57.

The authors stress the extremely high mortality rate of untreated bronchiectasis. Various series show a mortality rate of from 26 to 66 per cent. The morbidity of chronic bronchiectasis is pointed out. The onset of bronchiectasis can be traced to childhood in about 40 to 60 per cent of the cases. The mortality of surgical treatment of bronchiectasis in children and infants is low, about 1 to 2 per cent.

The authors believe that early diagnosis and surgical extirpation of the disease should be obtained whenever possible.

Two infants developing bronchiectasis while under observation are described. In both, bronchial obstruction with infection was the apparent cause. In one infant the obstruction developed in connection with an unexpanded lower lobe. In the other, the obstruction was associated with the depression accompanying a tuberculous meningitis. Both were completely relieved of their pulmonary disease by operative extirpation.—*Thomas C. Stansbury, M.D.*

KARANI, S. Kartagener's syndrome. *Brit. M. J.*, July 12, 1952, *1*, 74–75.

Attention was first called to the association of bronchiectasis with sinus maldevelopment and transposition of viscera by Kartagener in 1933, and his name has been attached to this syndrome. As case reports accumulated, a strong hereditary tendency became evident. The author reports the syndrome in 2 sisters among 4 siblings, the first report of familial occurrence in the British literature.

The association of bronchiectasis with congenital anomalies leads to speculation as to whether the primary cause of the bronchiectasis in these individuals, as well as in many persons who do not have obvious anomalies, may not be a congenital defect of the bronchial wall. Cases of dextrocardia and bronchiectasis without sinus infection have been reported. Cases of bronchiectasis in otherwise normal individuals without evidence of upper respiratory infection or bronchial obstruction have also been reported. It seems rather likely that in many instances upper respiratory infection is a contributory factor in bronchiectasis with weakness of the bronchial wall the primary cause.—*George Cooper, Jr., M.D.*

SOMMER, F., and REINHARDT, K. Das diagnostische subseröse Emphysem. (Diagnostic subserous emphysema.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1952, *77*, 54–62.

A pneumoperitoneum as a diagnostic procedure is not without danger. The authors found 8 fatal cases due to its use in the literature. They believe it should be employed only in exceptional cases. Pneumography of the kidneys by retroperitoneal injection of air is also complicated by dangerous sequences in some instances.

A different method of using air for the demonstra-

tion of abdominal and retroperitoneal organs is the injection of air into the presacral space first described by Ruiz Rivas. The authors have used the method in 20 cases. From 1,000 to 1,600 cc. of air or oxygen is aseptically injected into the loose presacral and periproctal tissue. The patient is in a kneeling position and supports the body on the elbows. General anesthesia is not necessary. One must of course make sure that no blood vessel has been entered.

No complications were noted and none were reported in the available literature, except puncturing the rectum which led to no serious consequences.

The air injection produces an emphysema of the subserous spaces. This fact allows the demonstration of the kidneys, liver, spleen, suprarenals, pancreas, mesentery and some of the pelvic structures. The kidneys are demonstrated most efficiently; in all of the 20 cases there was a good air outline of the kidneys.

This type of examination seems indicated in cases of tumors, cysts, hydronephrosis, etc. For demonstration of the adrenals the diagnostic subserous emphysema in combination with laminagraphy is almost always satisfactory. The method is of help to determine the size of liver and spleen. Occasionally the gallbladder is seen. Stomach and colon can be demonstrated when they are filled with air. When this is done the pancreas can be seen in the majority of instances. The pelvic organs can usually be outlined well. The uterus, the round ligament and the ovaries are surrounded by air. The mediastinum contains air after this procedure. When laminagraphy is used it is often possible to demonstrate the thoracic aorta and the pulmonary artery more accurately than on plain laminagrams.—*Hans W. Hefke, M.D.*

Cooke, Francis N., and Blades, Brian. Cystic disease of the lungs. *J. Thoracic Surg.*, June, 1952, *23*, 546–569.

There is much confusion as to the classification and nomenclature of cystic disease of the lung. The authors suggest the following classification:

I. Congenital Pulmonary Cysts.
  A. Bronchogenic cell type
    1. Solitary
    2. Multiple
  B. Alveolar cell type
    1. Solitary (balloon cyst, pneumatocele)
    2. Multiple
  C. Bronchogenic and alveolar types combined
II. Acquired Pulmonary Cysts.
  A. Bullous emphysema
  B. Subpleural blebs.

The authors believe that the use of this or another standard classification would facilitate statistical analysis and help clarify much of the confusion in regard to prognosis and treatment. A discussion of the classification, both anatomic and histopathologic, is given.

They report 10 representative cases including reproductions of roentgenograms, photographs of gross specimens and photomicrographs. Considerable emphasis is placed on the problems encountered in the surgical management.—*Thomas C. Stansbury, M.D.*

Felson, Benjamin. Acute miliary diseases of the lung. *Radiology*, July, 1952, *59*, 32–48.

The presence of disseminated miliary lesions in the lungs has been reported as occurring in over 80 different conditions. The author briefly discusses about half this number which have come under his personal observation.

The diseases are classified as acute, subacute or chronic, dependent upon the rate at which a *striking* change, progressive or regressive, is visualized on serial roentgenograms.

The roentgen appearance, pathology and clinical aids concerning various diseases are described and discussed under the following headings: (A) bacterial infections; (B) virus and rickettsial infections; (C) fungus infection; (D) parasitic infections; (E) noxious inhalations; (F) diseases with variable etiology; and (G) diseases of uncertain etiology. Contrary to the author's hope, a study of the characteristics of the individual nodules gave no clue to the diagnosis.

A table is included to aid in the differential diagnosis of the commoner type of acute miliary diseases. The author believes that with the aid of certain clinical and laboratory data and serial roentgenograms, a more accurate and narrowed differential diagnosis can usually be established. Twelve good figures of chest roentgenograms depicting various miliary lesions are included.—*Everett E. Seedorf, M.D.*

Ballantyne, Alando J., Clagett, O. Theron, and McDonald, John R. Extrapulmonary oil granulomas secondary to oleothorax. *Proc. Staff Meet., Mayo Clin.*, June 18, 1952, *27*, 250–255.

There have been many reports on the development of oil granulomas secondary to the use of solid and liquid paraffins in medical and surgical procedures, including the injection treatment of hernias and hemorrhoids, the correction of defects about the face and neck, and in the peritoneal cavity to prevent the development of adhesions after surgery.

The authors cite 3 cases in which extrapulmonary paraffinomas occurred after the installation of mineral oil into the pleural space as an adjunct in the collapse therapy of pulmonary tuberculosis. In all of these cases, it is pointed out, oil granuolmas may appear a number of years after the oil instillation. The granulomas had occurred secondary to migration of a portion of the oil from the intrapleural space; the significant spread was thought to take place along tissue planes such as those followed in

the development of subcutaneous and mediastinal emphysema.

In the first patient the granuloma appeared as a recurrent mass in the left breast, with attachment and fixation to the surrounding tissues. In the second case the tumor surrounded the roots of the right brachial plexus, with resulting neurologic manifestations. The initial complaint in the third case was difficulty in swallowing, and a mediastinal oil granuloma was found which encroached upon the esophagus. Histopathologic studies proved the diagnosis in 2 of the cases; in the other, in which there had been involvement of the brachial plexus, it was not possible to remove tissue for study, but the sequence of events pointed to a paraffinoma. Each patient was submitted to surgery, but only in the case of breast involvement was excision of the tumor possible. It should also be noted that in this patient the tumor became manifest a number of years after the oil had been removed from the pleural space. Removal of the residual mineral oil from the thorax was carried out in each case.

The authors warn that whenever mineral oil is employed, the possibility of development of an oil granuloma must be considered. They also express the opinion that any patient for whom oleothorax has been established should be examined frequently, because the appearance of effusion beneath the oil or the fibrosis and contraction of the pleura occasioned by the oil may lead to an increase in the intrapleural pressure and thus cause extrapleural migration.—*Carson R. Jones, M.D.*

Löffler, W., Essellier, A. F., de Meyer, G., and Morandi, L. Flüchtige Lungeninfiltrate mit Bluteosinophilie nach therapeutischen Ölinjektionen. (Transient lung infiltrations and blood eosinophilia following therapeutic oil injections.) *Schweiz. med. Wchnschr.*, Aug. 2, 1952, *82*, 777–785.

The authors present 4 cases in which manifestations similar to Loeffler's syndrome developed after injection of such vegetable oils as peanut oil, oil of almonds, and olive oil as vehicles for antiobiotic medication.

The lung changes consisted of fine and coarse nodular infiltrations of hematogenous distribution, hilar enlargement, and an occasional pleural effusion.

Blood eosinophilia as high as 83 per cent followed shortly after the lungs were involved and was probably due to a resorptive inflammatory response to the tissue lipase in the oil depots.

The pulmonary findings are attributed to microembolization of oil droplets from the sites of intramuscular injections. In 1 patient the lung and blood findings paralleled the increase or decrease in amount of oil injected.—*Joseph Zausner, M.D.*

Eidinger, Stanley L., and Rubin, Eli H. Spontaneous pneumohaemothorax; report of three cases. *Canad. M. A. J.*, July, 1952, *67*, 43–46.

Three additional cases of a relatively uncommon condition are reported, illustrating the usual clinical features of the syndrome of spontaneous pneumohemothorax which usually occurs in a young, otherwise healthy individual. Sudden chest pain and dyspnea may subside, subsequently to recur, followed by fever and shock.

Treatment after the acute phase should be directed towards re-expansion of the lung, and fibrinolytic agents or even decortication may be necessary because of infection and/or organization.—*W. J. Canada, M.D.*

Schaefer, George, and Epstein, Harry H. Lobectomy for pulmonary tuberculosis during pregnancy. *Am. J. Obst. & Gynec.*, July, 1952, *64*, 188–193.

Surgical procedures such as thoracoplasties and lobectomies can be performed on pregnant women suffering from tuberculosis without deleterious effect on the course of their pregnancy.

Radical lung surgery is not advocated after the seventh month of gestation as there is the danger of a premature labor. In these cases it is best to carry the patient along with streptomycin and para-aminosalicylic acid. Although some do hold that streptomycin given during pregnancy may cause eighth nerve deafness to the infant, this has not been the experience of the authors. They have under observation several infants now over two years of age whose mothers had received streptomycin during the entire period of gestation.

The authors have a series of 6 patients who have delivered following lobectomy or pulmonary resection performed after the onset of pregnancy and report a case in which lobectomy was performed during the first trimester of pregnancy.—*Joseph Levitin, M.D.*

Weiss, William, and Stecher, William. Tuberculosis and the sickle-cell trait. *A.M.A. Arch. Int. Med.*, June, 1952, *89*, 914–922.

Sicklemia (the sickle-cell trait) is found in a significant number of Negroes—7.25 per cent of the Negroes in the United States. The authors have shown it to be more than twice as common (12.6 per cent) among tuberculous Negroes admitted to a large muncipal hospital than among nontuberculous Negroes admitted to the same hospital (5.3 per cent). They have also shown that exudative tuberculosis is twice as common among tuberculous Negroes with the "sickling trait" (74 per cent) as among tuberculous Negroes without the trait (38 per cent).

It is suggested that the presence of sickle cells in the pulmonary arterial blood may tend to obstruct

the flow of blood through the capillaries because of the pointed shape of the cells. Therefore, less oxygen is taken up from the alveolar air per unit of time. This would leave a greater amount of oxygen available in the alveolar air. The tubercle bacillus is an aerobe and, within certain limits, grows better in atmospheres of higher oxygen tension. The tubercle bacillus may therefore grow better and multiply faster. Thus, the lobular pneumonia of the initial tuberculous infection would assume greater proportions in a person with the sickling trait and would lead to an increased incidence of clinical tuberculosis, particularly exudative tuberculosis, in these persons. —*Chauncey N. Borman, M.D.*

Schoenmackers, J., and Vieten, H. Das postmortale Angiogramm der Lungen bei Tuberkulose, Silikose and Bronchialkarzinom. (The postmortem angiogram of the lungs in cases of tuberculosis, silicosis and bronchogenic carcinoma.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1952, *77*, 14–28.

For a better understanding of the anatomical variations in the three diseases mentioned in the title, the authors have studied the vascular changes in the lung fields by executing postmortem angiograms. The pattern associated with the three conditions is dependent upon the aeration of lung, thoracic form and the position of the diaphragms. These conditions may show a variation in the amount of vascularity. The branches of the pulmonary arteries may be displaced, actually destroyed or partially or entirely compressed. When adhesions occur between the lung and pleura, intercommunicating vessels may actually develop. The authors point out that the same vascular changes may occur in pneumonia, pulmonary abscesses, gangrene, bronchiectasis, embolism and metastasis.

Thus the various changes mentioned cannot be considered characteristic of any one of the three diseases mentioned in the title. In fact they are very similar and are what one would have expected from the pre-existing knowledge of the anatomy of the particular disease. The results are interesting anatomical studies, but perhaps have not too much practical value.—*Paul C. Swenson, M.D.*

Black, Harrison, and Ackerman, Lauren V. The importance of epidermoid carcinoma *in situ* in the histogenesis of carcinoma of the lung. *Ann. Surg.*, July, 1952, *136*, 44–55.

The concept of carcinoma *in situ*, *i.e.*, intra-epithelial cancer without invasion of underlying tissues, is reviewed and the evidence for the progression of carcinoma *in situ* of the cervix to frankly invasive carcinoma is briefly discussed, the sequence apparently being: (1) hyperactivity of the basal layer, (2) epidermoid carcinoma *in situ*, and (3) invasive epidermoid carcinoma.

The association of marked squamous metaplasia of the bronchial epithelium and ducts of the mucous glands with carcinoma of the lung has been described by a number of investigators but since this is also observed with a variety of chronic pulmonary disorders which are not commonly precursors of lung carcinoma, the association is regarded as an interesting coincidence. However, the authors have noted that when increased activity of the basal cell layer is present, frank invasive carcinoma is found at some nearby site in a significantly large number of cases. In a series of 60 cases of epidermoid and undifferentiated carcinoma of the lung removed at operation, carcinoma *in situ* was present in adjacent areas in 13 (22 per cent) and anaplastic hyperactivity of the bronchial epithelium was found in an additional 8 (13 per cent).

The process appears to begin with increased mitotic activity in the basal layer followed by dense packing of nuclei and increased stratification. As the process advances the basal cell activity extends closer to the surface. Complete epidermidalization with intra-epithelial pearls probably immediately precedes frank epidermoid carcinoma *in situ*. The authors' criteria for the latter condition are as follows: (1) absence of cellular differentiation and organization; (2) variation in size and shape of the nuclei with nuclear hyperchromatism; (3) increase of the nuclear-cytoplasmic ratio; (4) increased number and abnormal forms of mitotic figures; (5) above changes seen extending through all layers to the surface; (6) intact basement membrane.

Of particular interest is the fact that multiple areas of preinvasive malignant change were found at some distance from resected tumors and in 2 cases carcinoma *in situ* was demonstrated in the lung opposite the main tumor. Because of the multicentric origin of these changes, the question is raised whether bronchogenic carcinoma should ever be treated by lobectomy when carcinoma *in situ* is demonstrated, even if the lymph nodes are negative at operation.

The authors also broach the question as to what course should be followed when a bronchial biopsy is reported as epidermoid carcinoma *in situ*. They conclude that in those cases where the clinical findings favor bronchogenic carcinoma, exploratory thoracotomy is justified.—*Martin B. Levene, M.D.*

Gros, C. M., Sigrist, R., and Veillon, A. Le radiodiagnostic du sein. (Roentgen diagnosis of the breast.) *Gynéc. et obst.*, 1952, *51*, 228–235.

Two techniques are mentioned the first of which is considered more important and much simpler to perform. The authors report 3 cases of breast tumor de-

scribing their roentgenographic findings (clinical and histogical data corroborating).

The technique consists simply of soft tissue roentgenography with 30 to 50 kv., having compressed the breast uniformly with a special spot film device, thus enabling the use of fluoroscopy for localization of the tumor density and serial roentgenography of various incidences.

It is also pointed out that in cases of bleeding of the nipple it is possible to inject the lactiferous ducts with a radiopaque material such as diodone, being sure, however, the bleeding is not due to a mastitis.

The authors conclude that even though no characteristic roentgenographic description of the benign and malignant tumors of the breast can be given as yet, it is possible to differentiate certain malignant tumors because of their irregular borders, numerous punctiform calcifications and non-homogeneous density.—*Jirair N. Sarian, M.D.*

Gershon-Cohen, J., and Ingleby, Helen. Roentgenography of fibroadenoma of the breast. *Radiology*, July, 1952, *59*, 77–87.

Fibroadenomas of the breast are benign hormone influenced tumors which are seen frequently in the adolescent or young adult. The authors obtain a roentgenogram in the lateral and tangential view of each breast. A small lead shot is placed on the skin over the tumor area for localization. Since a fibroadenoma has the same density as normal breast tissue, there must be either a natural or an artificial contrast medium in order to see the tumor. Fat in the breasts is a good natural contrast medium, and in those breasts where it is present a fibroadenoma becomes discernible. In the compact adolescent, mazoplastic or pregnant breast these tumors are not visualized, although they may be partially visualized where the tumor projects into the subcutaneous layer of fat or where there is sufficient fat invasion to serve for contrast purposes. When they are of large size or there is a high fat content of the breast they are completely visualized. A palpable tumor in an adolescent or young adult not seen on the roentgenogram is apt to be a fibroadenoma.

Typically the density of fibroadenoma is uniform; the margins are smooth; the contour is often lobulated or bosselated and the perifocal tissues are pushed aside rather than invaded. When calcification occurs it assumes all sorts of bizarre forms and tends to be irregular and coarse.

The differential diagnosis must include cysts, and as many fibroadenomas undergo cystic or mucous degeneration, they resemble cystic lesions more than any other breast lesion. Papilloma is suspected when an elongated tortuous subareolar duct is visualized. Secretory cystic disease with plasma cell mastitis has flame-like stromal digitations streaming backward from the areolar area and the coarsely tentacled mass of plasma cell mastitis is quite different from the smoothly contoured fibroadenoma. Carcinoma has a spiculated or tentacled margin; calcification, if present, is finely granulated and differs from the coarse and bizarre calcification seen in fibroadenoma. Secondary signs of malignant tumors, such as dimpling, retraction or edema of the skin are seldom seen. —*Donald N. Dysart, M.D.*

Abdomen

Lidén, Kurt, and Lindgren, Martin. Radiation hazards during cholangiographic examinations. *Acta radiol.*, July, 1952, *38*, 1–7.

In Sweden the radiologic safety dose is considered to be 100 milliroentgens a week. Radiation measurements during cholangiographic examinations at Lund showed that all assistants standing 3 meters from the irradiated field received such a small amount of radiation that no special protective measures were necessary. However, it was found that the upper part of the anesthetist's body was exposed to relatively large amounts of radiation.

Therefore, a protective lead rubber shield with a lead glass window was designed and control measurements showed that it completely fulfilled its purpose of absorbing the scattered radiation.—*Mary Frances Vastine, M.D.*

Leger, Lucien, Zara, Marcel, and Arvay. Cholangiographie et drainage biliaire par ponction trans-hépatique. (Cholangiography and biliary drianage by means of transhepatic puncture.) *Presse méd.*, June 18, 1952, *60*, 936–937.

The authors have used the method described by Carter and Saypol in the *Journal of the American Medical Association* (1952), injecting diodone into an intrahepatic duct by means of a lumbar puncture needle. In the presence of obstructive jaundice, when the biliary ducts are dilated, it is relatively easy to puncture one of the intrahepatic ducts, obtain flow of bile and inject a contrast medium.

Two cases in which the method was used successfully are reported. Injection can be performed either preoperatively or during laparotomy. The report, illustrated with roentgenographic reproductions, confirms the findings of Carter and Saypol.—*Albert Oppenheimer, M.D.*

Aird, Ian. The surgical aspects of intrahepatic biliary obstruction. *Ann. Surg.*, July, 1952, *136*, 27–38.

It is not entirely rare to see patients who by all available clinical tests are shown to be suffering from obstructive jaundice, and are found on exploration to have no extrahepatic biliary obstruction. When this situation arises, it is the author's practice to use operative cholangiography as a measure of determin-

ing the presence and nature of the intrahepatic obstructing lesions.

Under separate pathological headings, 6 cases of intrahepatic biliary obstruction are recorded, due to intrahepatic stones, hepatoma arising near the porta hepatis, and very extensive malignant infiltration of biliary passage within the liver.

Some patients presenting a clearcut picture of obstructive jaundice may show no detectable biliary obstruction and may provide a normal operative cholangiography. It seems justifiable to use the term cholangiolitic biliary obstruction in such cases.—*C. C. Wang, M.D.*

Livingston, Harold J., and Livingston, Saul F. "Re-formed gall bladder" with stones following cholecystectomy seventeen years ago. *A.M.A. Arch. Int. Med.*, June, 1952, *89*, 961–966.

The reappearance of abdominal symptoms following cholecystectomy frequently provides a source of distress to both patient and physician. Various diagnoses such as postcholecystectomy syndrome, spasm of or stones in the common duct, strictures or angulation of the extrahepatic ducts, chronic hepatitis, chronic pancreatitis and neurogenic factors are lightly proffered without adequate substantiation, and usually symptomatic therapy is instituted. The proper assessment of the many potential alterations in the postoperative biliary tract is essential. The entity of "re-formed gallbladder" is not unknown to the medical literature but its frequency and subsequent misdiagnosis serve to demonstrate that this concept has not been adequately popularized.

A case of "re-formed gallbladder" with stones following cholecystectomy seventeen years ago is presented. The re-formed stones were demonstrated by roentgen examination and the gallbladder was subsequently removed, the presence of four calculi being verified.

Any obstruction at the junction of the dilated remnant of the cystic duct and common duct, the secreted material with bile accumulating behind the obstruction, may be sufficient to initiate the reformation of a "gallbladder" like structure. In time, the presence of mucoid material and stagnant bile in the pouch-like stump of the cystic duct may be followed by infection, inflammation and, at times the formation of stones. The process may also be initialed by cystic duct calculi which are missed by palpation and probing during the original operative procedure because of the tortuosity of the duct and the presence of the spiral valves of Heister.

The more common disturbances of the biliary tree such as injury to the major ducts, angulation of the common duct following ahesions, and common duct stones must be considered and ruled out in the differential diagnosis. Failure to visualize the "reformed ballbladder" with roentgenograms does not rule out its presence. It can or may be identified only by reoperation and careful dissection of all ducts.

Prophylactically, the surgeon, when performing cholecystectomies, should make every effort to ligate the cystic duct close to its junction with the common duct.—*Chauncey N. Borman, M.D.*

Bovill, E. G., and Bailey, W. J. Annular pancreas; report of a case. *J. Michigan M. Soc.*, July, 1952, *51*, 837–842.

Annual pancreas is a developmental anomaly in which a firm ring of normal pancreatic tissue completely encircles the descending portion of the duodenum. This is continuous with the head of the pancreas without any anatomical delineation.

This anomaly may be asymptomatic, and eventually an incidental autopsy finding, or it may produce clinical symptoms of incomplete duodenal obstruction due to constriction of the descending portion of the duodenum. Dilatation and hypertrophy of the proximal duodenum and frequently of the stomach may result. The annual pancreas cannot be distinguished histologically from the normal pancreas.

A total of 67 cases have been reported in the literature; 39 were found at autopsy and 28 cases came to surgery. The ages varied from the newborn period to seventy-four years. The clinical findings in all 28 cases which came to surgery were those of acute or chronic duodenal obstruction. Roentgen examination was performed on 21 cases. All had partial or complete obstruction of the second portion of the duodenum, and in 14 cases an associated dilatation of the first portion was noted.

The surgical procedures used were (1) a direct attack on the constricting ring, (2) a short-circuiting anastomosis around the obstruction by means of gastrojejunostomy with or without gastric resection, duodenojejunostomy and duodenogastrostomy, and (3) a combination of both.

The authors report the case of a twenty-six year old male who was admitted to a Veterans Administration Hospital on September 22, 1950. He had been discharged from the Navy because of "stomach trouble," and had since maintained a bland diet. For five weeks prior to admission he noted loss of appetite and epigastric pain, relieved by vomiting. Vomiting of blood and melena were noted on three occasions. Past history was noncontributory.

Excepting for undernourishment and underweight the physical examination was negative. Free gastric acidity was 51, total acidity was 68.5. Roentgen studies revealed narrowing of the postbulbar segment of the duodenum, with spasm of the duodenal cap. There is no gastric residue.

At operation a peritoneal fold was found extending from the liver border to the lesser omentum and hepatic flexure, obscuring the gallbladder and the porta hepatis. When this fold was incised, it was seen that the pylorus ended in the center of a mass of

pancreatic tissue. This completely surrounded the duodenum and was continuous with the head of the pancreas. This mass was dissected from the duodenum to about 3 cm. from the pylorus, but as the location of the terminal biliary and pancreatic ducts was not known, it was stopped at this point. The duodenum was small, being 1.3 cm. in its external diameter, and 0.7 cm. in its internal diameter. The mass encircled the first and second portions of the duodenum. Subtotal gastric resection was performed (anterior Pólya-Hoffmeister). The patient made a complete recovery and left the hospital on November 2, 1950.

Tabulation of the pertinent findings in the 28 operated cases reported in the literature and several diagrams are presented with the article.—*William H. Shehadi, M.D.*

CAMERMAN, J. L'hépatosplénographie; résultats obtenus au moyen d'un nouveau produit de contraste. (Hepatosplenography; results obtained by means of a new contrast substance.) *J. belge de radiol.*, 1952, *35*, 512–518.

The author uses ethyl diiodostearate in a suspension with a particle size of about 2 microns. The material is known as Angiopac (Meurice). It is injected by vein or artery; 20 cc. in an average size patient gives rather faint visualization of the spleen but 30 to 40 cc. gives good visualization. The spleen becomes opaque in about fifteen minutes, lasting about five hours. Best results are obtained one to three hours after injection. There may be a faint residual density after twenty-four hours but none after forty-eight hours. Results with intravenous and intra-arterial injection do not differ.

With these doses, the liver and lymph nodes are not opacified. In the animal 2 cc. per kg. is required, whereas the dose for splenic visualization is about 0.5 to 0.75 cc. per kg.

On rare occasions there have been untoward reactions such as shivering, cyanosis and headache one-half to one hour after injection. One or 2 patients complained of a serous rhinitis. These complaints disappeared following the administration of adrenalin. These reactions are not thought to be due to embolism and did not occur after injection of the carotid artery. Arteriosclerosis is not a contraindication. The patients in the poorest condition withstood the procedure poorly but gave the best visualization. Sensitivity to iodine is probably a contraindication as is narcosis and spinal anesthesia. These contraindications should be heeded, particularly when larger doses are used to visualize the liver. It is believed that splenography should not only give information about the size and shape of the organ but also evidence of tumor, infarction, cyst, abscess, accessory spleen, etc.—*Marcy L. Sussman, M.D.*

RAVITCH, MARK M., and HANDELSMAN, JACOB C. Defects in right diaphragm of infants and children with herniation of liver. *A.M.A. Arch. Surg.*, June, 1952, *64*, 794–802.

Hemispherical bulging of the right diaphragm into the thorax is fairly commonly revealed roentgenologically in children. The term eventration is usually applied; this includes a large group where elevation exists secondary to phrenic palsy, and the rare case where the diaphragm is replaced by a thin nonmuscular membrane. The 5 cases here discussed apparently belong to the latter group but only a section of the diaphragm which is normally muscular is involved.

The involved area is central, circular, well defined, and ringed by normal diaphragmatic muscle. The size varies from one-half the area of the right diaphragm to 4.0 cm. diameter; the smaller the lesion, the more the similarity to a true diaphragmatic hernia, as the surrounding normal phrenic muscle acts as a ring within which the thinned-out membrane bulges into the thorax under abdominal pressure as does a hernia sac.

Anatomically and clinically such a lesion is indistinguishable from a congenital diaphragmatic hernia and is subject to the same complications of pressure on lung or strangulation of abdominal content within the thorax. In all 5 cases herein described protrusion of liver was present. Three of the 5 presented initially a respiratory complaint which disappeared or was altered after operation. Surgical correction is readily carried out transthoracically and consists of plication of the membranous bulging area.

Biopsy in 3 cases revealed "muscle" or "scarred muscle," and in 1 case fibrous tissue indistinguishable from tendinous portion of diaphragm. This suggests that the underlying pathological condition may be a localized affection of diaphragmetic innervation.

This condition should be considered in the differential diagnosis of masses low in the right chest that are roentgenologically sharply demarcated superiorly and not separable from the diaphragm inferiorly. Operation is the recommended treatment in all cases for the same reasons that it is indicated in the usual cases of diaphragmatic hernia.—*William C. MacCarty, Jr., M.D.*

PHILIPP, ELLIOT E., and SKELTON, M. O. Congenital diaphragmatic hernia in siblings. *Brit. M. J.*, June 14, 1952, *1*, 1283–1284.

True congenital diaphragmatic hernia is a relatively uncommon anomaly, and its occurrence in siblings has been reported only once previously (Makela, 1916).

A German woman, aged nineteen, was admitted to the hospital in 1948 for pre-eclamptic toxema and hydramnios necessitating induction of labor at thirty-six weeks. Forceps delivery was performed due to maternal distress and the occipitoposterior position of the vertex. The infant, a boy weighing 6

lb. 14 oz. (3.1 kg.), gasped for about twenty minutes after birth, and then died. At necropsy there was a massive left-sided diaphragmatic hernia. The stomach and intestines. from the ileum to the transverse colon, were located in the thorax, together with the spleen and the left lobe of the liver. The left lung was collapsed with considerable displacement of the mediastinum to the right. Two-thirds of the liver, the duodenum, the pancreas, and kidneys remained in the abdominal cavity. No other congenital defects were found.

The patient became pregnant for the second time in 1951. At thirty-three weeks she was admitted with severe vomiting and moderate edema of the ankles; her blood pressure was 150/110. By thirty-eight weeks it had risen, and there was marked edema of the ankles, face and abdominal wall. No albuminuria was present at any time.

After a medical induction at thirty-nine weeks, she gave birth to a male child; its condition at first was good, but it rapidly deteriorated about ten minutes after birth, when it became cyanosed and limp. Oxygen was administered unsuccessfully, and he died nineteen hours after birth.

Necropsy showed a massive right-sided diaphragmatic hernia through a large posterior defect in the diaphragm. The small intestine, spleen, ascending colon, right half of the transverse colon, and pancreas were again located in the thorax. The greater part of the liver was in the abdominal cavity, but a large lobulated mass of liver tissue was present in the thorax, attached to the main mass by a narrow isthmus of fibrous tissue. Sections of the liver, adrenal, pancreas, and myocardium were normal.

Severe congenital diaphragmatic hernia is calculated to occur once in 23,000 deliveries, but lesser defects of the diaphragm are more common. Although there is no known definite history of congenital defects of this or any other type in either the mother's or the father's family, it seems likely that these two identical uncommon congenital defects may be due to some inherited genetic trait.

How far dietary deficiencies could have played a part in this case is not known, though it is likely that the patient lived on a notably deficient diet during puberty and adolescence in Germany. The occurrences of toxemia and hydramnios in both pregnancies may also be significant.

The true condition of the second child might have been diagnosed in view of the previous history of diaphragmatic hernia. Such an occurrence in successive pregnancies is obviously rare. The chances of the patient having a third similarly affected child are unknown; they are probably high.—*Stephen N. Tager, M.D.*

Watkins, David H., Harper, Fred R., and Condon, William B. Diaphragmatic hernias with visceral complications. *A.M.A. Arch. Surg.*, July, 1952, *65*, 95–108.

The authors present a series of 5 cases of diaphragmatic hernia with serious visceral complications. Each case report gives a concise medical history, the physical and roentgenographic findings (illustrated), operative findings, and postoperative course.

Case 1 is that of a strong well developed man, thirty-one years old, who was injured in a head-on automobile accident. He was unconscious for forty-eight hours afterward. Three weeks later he was seen by the authors because of dyspnea, intermittent cramping abdominal pain, and pain in the left shoulder. A diagnosis of traumatic left diaphragmatic hernia was made. At surgery, the stomach, small intestine, colon, omentum, and left lobe of the liver were found in the thorax. No hernial sac was present. An interesting finding was a complete tear across the anterior mediastinum. Thus, both lungs were partially collapsed. The tear in the diaphragm was found to extend from a point 2 inches to the left of the xiphoid process through the esophageal hiatus. After replacement of the abdominal viscera, the esophageal hiatus was reconstructed and the diaphragm repaired with silk mattress sutures. No attempt was made to close the mediastinal pleura. The lungs were fully re-expanded before closure of the thorax. The patient's postoperative course was uneventful. Follow-up roentgenograms have shown no recurrence of the hernia.

The second case report is that of a forty-two year old white man, a schoolteacher, with complaint of sudden onset of pain in the entire left chest which radiated down the left arm. The pain had persisted constantly and had become unbearable. He was unable to take a deep breath, to cough, or to raise his left arm. He had undergone a sympathectomy for hypertension one year previously. Roentgen examination showed that the right lung was clear, the heart was enlarged, and the left diaphragm was not visualized. There was thought to be a left lobar pneumonia. The patient was treated with antibiotics and chemotherapy. Fever and pain persisted. Eight days later, a follow-up roentgenogram showed the left chest to be entirely radiopaque which was interpreted as being due to fluid. The heart and mediastinum were displaced tl the right. At surgery, both the visceral and parietal pleural surfaces were very red and covered with fibrinous exudate. Beneath the left lower lobe a portion of strangulated stomach, dilated, black, and with multiple perforations was found above the diaphragm herniating through a 1 inch opening. The postoperative course was stormy and a residual empyema was found. One month after the thoracotomy, decortication of the left lung performed. Subsequent convalescence was uneventful. The authors comment on this case by stating that with many cases of traumatic diaphragmatic hernias, the appearance of significant symptoms may be delayed and diagnosis difficult to estab-

lish. Postoperative hiatal hernias have followed transabdominal vagotomy and gastric resection performed for peptic ulcer.

CASE III is that of a forty-three year old white male who had been thrown against the dashboard during an automobile accident. The original roentgen examination revealed fractures of multiple ribs on the right side with a slight amount of fluid in the right pleural space. One month after the automobile accident, the patient returned complaining of chest pain. Follow-up roentgenograms now showed a rounded hemogeneous density, apparently arising from the midportion of the right leaf of the diaphragm. Fluoroscopy with pneumoperitoneum gave the impression that this was loculated fluid rather than a diaphragmatic hernia. At surgery a herniation of the liver was found, presenting through a 10 by 12 cm. rent in the centromedial portion of the right diaphragm. There was no hernial sac. The postoperative course was uneventful.

Case IV describes a sixty-four year old white male whose complaint was inability to swallow solid food or liquids. He had been treated elsewhere for a duodenal ulcer in 1944 through 1946. For the past three years he had suffered almost continual heartburn and substernal distress. Eight weeks before admission, dysphagia developed and rapidly worsened. Roentgen examination of the esophagus showed the barium column stopped 2 inches above the normal position of the esophageal hiatus. The esophagus above the area of complete obstruction was smooth and somewhat dilated. Clinically, the impression was carcinoma. However, a biopsy showed chronic inflammatory tissue. At surgery, it was believed that the patient had an esophageal hernia with esophagitis and peptic ulceration of the esophagus which had progressed to stricture formation and shortening so that a secondary esophagus had resulted. Microscopic examination of the resected esophagus and stomach showed chronic ulcer of the esophagus with extensive fibrosis.

Case V represents an example of incarceration of viscera in a foramen of Morgagni hernia precipitated by postoperative distention. The patient, a sixty-five year old white man, was admitted to the orthopedic service for vitallium cup arthroplasty (June, 1951). On the thirteenth postoperative day following the second arthroplasty, upper abdominal distention, vomiting, and right chest pain occurred. Chest and abdominal roentgenograms demonstrated distended loops of intestine in the right thorax. A diagnosis of incarcerated hernia through the foramen of Morgagni was made. At surgery the hernia through the foramen of Morgagni was confirmed. The hernia contained one-half the stomach, the duodenum, the gall bladder, about 8 inches of the colon, and some loops of small bowel. The stomach was tremendously dilated, but there was no evidence of necrosis. A gangrenous portion of omentum and mesentery was removed. The postoperative course was uneventful.—*Ralph F. Niehaus, M.D.*

ALBOT, GUY, and TOULET, JACQUES. Relationship between histological lesions and radiological signs of cancers of the mucous membrane of the stomach. *Am. J. Digest. Dis.*, June, 1952, *19*, 161–168.

The authors present roentgenographic reproductions and specimen photographs to illustrate the early roentgenological signs of cancer of the stomach.

I. Histo-roentgenology of nonulcerated cancer of the mucous membrane:

(1) Demonstrated roentgenologically by the rigid stomach wall and lack of peristalsis through the lesion. The rigidity is produced by submucosal fibrosis with thinning of the mucosa centrally and thickening along the margin.

(2) Inches without ulceration are demonstrated due to the thinning of the mucosa and the rigidity of the wall through this area with contracture of the surrounding muscle. This can, at times, be accentuated by giving the patient a drug such as morphine.

(3) Modification of the perilesional profile of the mucous membrane; converging mucosal pattern radiating from the lesion with abnormal club shaped endings.

II. Histo-roentgenology of ulcerated cancer of the mucous membrane: In these, the findings are similar except there is a loss of the mucous membrane through the central area due to peptic digestion; the picture varies according to the stage of peptic digestion and the surrounding inflammatory reaction with edema.—*Vernon L. Peterson, M.D.*

PALUMBO, LOUIS T., PAUL, R. E., and WESTLY, G. T. Partial gastrectomy with and without vagus resection in treatment of duodenal ulcer. *A.M.A. Arch. Surg.*, June, 1952, *64*, 756–765.

A preliminary report is presented of a comparative analysis of 99 cases of partial gastrectomy followed from six to fifty-four months, and 30 cases of partial gastrectomy combined with bilateral infradiaphragmatic vagus resection followed from six to forty-eight months.

In both groups the duodenal ulcer was removed, and the type and extent (75 per cent) of gastric resection were identical. An antecolic gastrojejunal anastomosis with short afferent jejunal loop was employed. This procedure has not resulted in any obstruction to the transverse colon or interfered with normal stomal function and is simpler and less hazardous to perform than retrocolic anastomosis.

Postoperative mortality and complication rates were similar in the two groups—3 per cent and 30 per cent respectively. These are tabulated in detail. Two complications peculiar to the vagotomy are noted: dysphagia due to injury to the muscular layers of the lower esophagus and hemorrhagic pericarditis, probably traumatic, from mobilization of the vagus nerves.

Postoperative gastric analyses revealed absence of free hydrochloric acid in 91 per cent of the partial gastrectomy group, and 100 per cent of the gastrectomy-vagotomy group. In the former, gastric emptying time averaged one hour, in the latter four hours, and 33.3 per cent of this group showed hypermobility of the bowel by motor meal, with puddling, clumping, and segmentation of barium in the lower jejunum and upper ileum. Two patients (2.7 per cent) of the gastrectomy group developed marginal ulcer. Gastroscopy performed in 15 patients of the gastrectomy-vagotomy group revealed gastritis in 14, severe in 5. However, the majority had no complaints related to this. The dumping syndrome occurred with equal frequency (20 per cent) in both groups.

The over-all results were considered good to excellent in 87 per cent of the partial gastrectomy group and in 78 per cent of the gastrectomy-vagotomy group. Relief of pain, nausea and/or vomiting and weight gain was slightly more pronounced in the simple gastrectomy group. The most troublesome complication was diarrhea (30 per cent) in the gastrectomy-vagotomy group. No change was noted in the vagotomy effects over periods of up to four years.—*William C. MacCarty, Jr., M.D.*

Lunn, G. M. Carcinoma of the duodenum. *Brit. J. Surg.*, July, 1952, *40*, 5–12.

The discussion is mainly confined to the pathology and the surgical treatment of carcinoma of the duodenum. There is some controversy as to whether peripapillary lesions should be considered true duodenal growths. It is admitted that the ampulla several anatomical structures unite and it is usually impossible to decide from which growth started.

The author reports in detail diagnosis and treatment of 3 peripapillary carcinomas, 1 infrapapillary and 1 suprapapillary carcinoma. Four of the 5 cases were examined roentgenographically and 2 were diagnosed correctly.

The treatment of choice was pancreaticoduodenectomy for growths at or near the papilla of Vater, and segmental resection for the remainder. Patients are more comfortable if the pancreatic secretion is returned to the alimentary tract. There was 1 postoperative death. The remaining patients are well and free of recurrence six, eight, sixteen and twenty-six months after operation.—*E. A. Addington, M.D.*

Rogers, K. E., Goligher, J. C., and Williams, E. Rohan. Primary carcinoma of the third part of the duodenum. *Brit. J. Surg.*, July, 1952, *40*, 1–5.

It is the general impression that primary carcinoma of the duodenum, as contrasted with the secondary carcinoma due to invasion by growths originating in neighboring organs such as the pancreas, ampulla of Vater, and stomach, is an exceedingly rare lesion. It comprises only 0.3 per cent of all gastrointestinal malignancies.

This is a report of 2 cases in detail. Both cases illustrate well the typical symptomatology of this condition. In both, the main symptom was vomiting occurring at intervals of a few hours up to several days. It is wisely pointed out by the essayists that it might be well to accomplish the roentgen examination on patients with this type of symptomatology, and who have had previous negative studies, at a period when they are having their acute symptoms. Three previous roentgen examinations were negative on 1 of the 2 patients when examined during a lull period of symptoms.

One of the chief diagnostic difficulties is that the third portion of the duodenum is masked by the pars media of the barium-filled stomach in the erect and prone positions, but this masking is less in the supine position; further, compression may be applied to the anterior abdominal wall with the patient supine and the distal duodenum examined by fluoroscopy and spot films through the compressed and displaced stomach.—*E. A. Addington, M.D.*

Ravitch, Mark M. Consideration of errors in the diagnosis of intussusception. *A.M.A. Am. J. Dis. Child.*, July, 1952, *84*, 17–26.

In the period from 1939 to 1951, 79 children were treated for intussusception. Five deaths actually occurred in the first 40 cases which were treated between 1939 and 1946. In each instance, the delay which occurred before definitive treatment was caused by failure to diagnose the intussusception upon the patient's first visit to the hospital after the onset of the condition.

Errors in diagnosis were based upon a number of misconceptions. In some cases, a history of days or weeks of pain, vomiting, constipation, etc., with relative well-being, was not recognized as characteristic of chronic, nonstrangulating obstruction. In 6 cases, the passage of feces, even to the point of diarrheal stools, was enough to lead the examiners astray with the suspicion of dysentery. In several cases intestinal obstruction of uncertain type was thought to exist, but operation was not immediately undertaken. On the one hand, in many of the cases too much stress was laid on failure to feel a mass, while on the other hand, an enlarged "liver" was palpated in several cases, and insufficient weight was attached to a finding of slight abdominal tenderness or resistance. In some cases the absence of current-jelly stools apparently encouraged delay, but in others pink enema returns or a history of blood in the stools failed to alarm the observers.

The author recommends a ready resort to barium enema and plain roentgenograms of the abdomen in doubtful cases. A barium enema which runs into the distal ileum rules out the ordinary type of intussusception at the ileocecal valve but does not rule out one higher in the ileum. The latter will usually show distended gas-filled loops in the

roentgenogram. Mechanical intestinal obstruction from any cause requires early relief by operation. Alertness to advise early operation for suspected intestinal obstruction will benefit the patients with obstruction far more than it will harm the occasional patients who will prove to have been unobstructed. The author emphasizes the fact that occasional occurrence of "chronic," nonstrangulating, incompletely obstructing intussusception must be kept in mind.—*Ralph S. Bromer, M.D.*

FROEHLICH, A. L., and BUYSSENS, N. Contribution à l'étude des stéatorrhées. (Contribution to the study of steatorrhea.) *Acta gastroenterol. belg.*, June, 1952, *15*, 487–525.

This is a comprehensive discussion of steatorrhea with a detailed account of 12 cases of the idiopathic type, 3 cases following gastric surgery, 2 cases with anatomical disease of the small bowel and 2 cases with lamblia infestation. Only a brief summary of the outstanding features can be given here.

In Belgium, on a general medical service, there was, in two years, 1 case in 200 admissions. The disease is less rare than the small bowel diarrhea due to alterations in the external secretion of the pancreas secondary to chronic pancreatitis. It is more common in men. There is no evidence to support the thought that it is hereditary, congenital or that it follows celiac disease of infancy. The prognosis in those patients who appear in extreme cachexia with a loss of weight over 40 per cent of their ideal weight is very poor. Their symptoms have been present for many years and there is likely to be a fatal termination within three months. In those suffering merely from an intractable diarrhea and mild loss of weight, the onset is apt to be recent.

The early symptoms are loss of weight and diarrhea. Exceptionally, at the onset, there may be osteoporosis, a hemorrhagic syndrome or tetany. Signs of vitamin B deficiency are not frequent. Hyperchromic anemia may be found with a significant medullary erythroblastosis but no megaloblastosis. Vitamin D deficiency is more frequent but was clinically manifest in only 2 cases. It is important to recognize the existence of steatorrhea with constipation.

The chemical examination of stool, duodenal content and blood is considered in detail requiring study of the original paper.

Roentgenologically, hypertonicity and hypermotility are found but, in other cases, hypotonus and intestinal paresis may occur. The suggestion that paresis is of serious prognosis is not confirmed. It is more likely an index of increased mucous secretion which results in barium sedimentation. Acetylcholine was not found to be important, and, contrary to Ingelfinger's opinion, prostigmine was found to increase peristalsis and haustration.

Necropsy was performed in 4 cases. The findings included chronic infiltration of the mucosa with mononuclear cells and some fibrosis and degenerative changes of the small bowel.—*Marcy L. Sussman, M.D.*

MARTIN, JAMES F., and FRIEDELL, HYMER L. Partial obstruction of the small intestine; with special reference to the obstructing segment. *Radiology*, July, 1952, *59*, 49–62.

Partially obstructing lesions of the small bowel may be adequately studied in many cases by a routine barium meal, without resorting to more elaborate methods such as injection of the barium mixture through a duodenal tube, double-contrast examination, etc. Although in most cases the roentgen changes in partial obstruction are not absolutely specific, much accurate information may be obtained by carefully correlating the fluoroscopic and roentgenographic findings with particular attention to the obstructing segment, and to the bowel segment proximal to the point of partial obstruction.

In the segment proximal to the lesion, anatomical changes which may indicate the presence of a partial obstruction include: (a) gas within the lumen of the small intestine; (b) an increase in the caliber of the small intestine as identified by either a barium mixture or intraluminal gas; (c) abnormal mucosal pattern; (d) delay in the transit time of the barium column; (e) segmentation of the barium column; (f) abnormal position or mobility of the individual segments of the bowel; (g) abnormal peristaltic activity.

The obstructing segment is identified as a constant area of narrowing of the lumen which persists during peristalsis. In general, single short stenotic segments usually represent primary or metastatic neoplasms, while multiple short stenotic segments may represent chronic inflammatory lesions which have become fibrotic. Obstructive segments which are of greater length are likely to indicate inflammation. Other characteristics of the obstructing segment which are significant are: (a) mucosal pattern—which is destroyed in the case of carcinoma; edematous, and occasionally destroyed, by inflammatory lesions; unaltered by benign tumors, except at the base of the lesions; etc.; (b) contour of lesion—*e.g.*, carcinoma usually produces an irregular annular constriction; lymphosarcoma may cause an irregular constriction or actually a widening of the lumen; (c) peristalsis through the obstructing segment; (d) position of the lesion in the abdomen—*e.g.*, carcinoma occurs most frequently in the upper jejunum, lymphosarcoma is more common in the ileum.

A number of cases of partial obstruction of the small intestine are presented, with the results of examination by serial films, fluoroscopy, and spot roentgenograms.—*Lynne Taylor, M.D.*

Milch, Elmer, Mendez, F. L., Jr., and Murphy, Harry. Recurrent gallstone small bowel obstruction. *A.M.A. Arch. Surg.*, June, 1952, *64*, 847–850.

Small bowel obstruction due to gallstone in the intestine is more common than usually thought. At the Buffalo General Hospital in the five years from 1946 to 1951, 8 of 217 cases of complete small bowel obstruction were due to gallstones, an incidence of 3.6 per cent.

Recurrence of obstruction due to a second stone contained within the gallbladder at the time of initial surgery are rare. The authors add 1 such case to 5 previously reported.

Gallstone ileus should be suspected when, in the presence of clinical small bowel obstruction, there is roentgenographic evidence of gas in the biliary radicles, with or without demonstration of an opaque density within the dilated loops. The diagnosis should be especially considered in elderly patients on whom no previous laparotomy has been performed.

Early diagnosis and operation are imperative to reduce the mortality rate, and correction of the existing biliary pathology as soon as feasible prevents additional complications. When no contraindications exist, the use of an oral contrast medium often aids demonstration of the enterocholecystic fistula.—*William C. MacCarty, Jr., M.D.*

Redish, Milton H. Ureteral complications and alterations of ureteral tonus in regional ileitis. *New England J. Med.*, June 26, 1952, *246*, 993–996.

Extravesical urinary tract complications of regional enteritis have not been adequately appreciated. The author's interest in this type of complication followed an evaluation of 2 cases in which urinary tract symptomatology was prominent.

In the first case, the patient gave a history of gastrointestinal complaints of six years' duration upon admission for right flank pain. Pyelography showed dilated right double ureters joining at sacroiliac level. At operation, the common right ureter was found to be incorporated in an inflammatory mass about the distal ileum involved by regional ileitis.

The second case had severe gastrointestinal symptoms and roentgen findings of severe regional ileitis. This patient was admitted three months following resection of a long segment of jejunum and ileum with sudden right flank pain. On physical examination there was right lower quadrant tenderness; pyelography showed a markedly dilated right ureter and right-sided hydronephrosis. These findings subsided with conservative therapy.

Routine pyelography in patients with regional enteritis was then instituted. In a series of 22 patients thus surveyed, 4 showed evidence of ureteral involvement. In each of these, dilatation of one or both ureters was found. In 1 instance a mild degree of hydronephrosis was noted. None of these 4 patients had genitourinary complaints.—*Israel R. Berger, M.D.*

Hillemand, P., Patel, J., Chérigié, P., Rosenstiel, R., and Manteau, Ph. Polypose adénomateuse du jéjunum et de l'iléon associée à une polypose adénomateuse colique droite et à deux gros polypes gastriques. (Adenomatous polyposis of the jejunum and ileum associated with adenomatous polyposis of the right colon and with two large gastric polyps.) *Presse méd.*, June 18, 1952, *60*, 911–913.

In a boy, aged fifteen, with a history of two episodes of intestinal obstruction, roentgen examination showed large polyps in the stomach and ascending colon, as well as multiple polyps in the jejunum and ileum.

Polyposis of the small intestine is rare; the authors found 67 recorded cases in the literature.

Clinically, intussception and volvulus seem to be the most serious complications.

The article is well illustrated with good roentgenographic reproductions, color photographs and photomicrographs.—*Albert Oppenheimer, M.D.*

Mondor, Henri, Porcher, Pierre, Olivier, Claude, and Simon, Gaston-Claude. Radio-diagnostic des volvulus du côlon droit. (Roentgen diagnosis of volvulus of the right colon.) *Presse méd.*, June 18, 1952, *60*, 901–905.

Twenty-four correct diagnoses among 69 cases of volvulus of the cecum, examined roentgenologically and described in the literature, indicates a distinct advance over previous purely clinical methods of examination. Furthermore, an analysis of the 69 cases suggests that the errors made were often not of observation but of interpretation.

The basic examination is made without preparation. The "immense gas balloon" described by Holubec in 1936 remains the major diagnostic sign. This can be demonstrated on the roentgenogram taken in decubitus, providing the entire abdomen is included. Contrary to the general impression, this unique and huge balloon which may be ovoid or kidney-shaped was found in the right hypochondrium only once in 6 cases. In 2 out of 6, it was prevertebral and, in the rest, about one-half of the cases, it was entirely to the left of the midline. Barium enema may be necessary to exclude a volvulus of the sigmoid.

Seven personal cases are presented.—*Marcy L. Sussman, M.D.*

GYNECOLOGY AND OBSTETRICS

BELL, J. SHERIDAN, and RAWLINGS, ARTHUR L. Roentgen fetal cephalometry. *Am. J Obst. & Gynec.*, June, 1952, *63*, 1371–1373.

A satisfactory simple method of roentgen fetal cephalometry that has been in use for four years is described.

An adjustable upright is fixed to a turntable. At the top of the upright is a saddle-shaped piece of wood in which is sunk a metal ball (ball bearing) 4.455 cm. in diameter. The upright and the ball are on the axis of rotation.

The mother stands astride the upright with the thighs pressed firmly against the piece of wood, which is at the perineum. A film is exposed. The turntable and the mother are rotated together 180 degrees. A second film is exposed. The selected diameter of the skull and the horizontal diameter of the ball are measured on each film, the shadows of the ball being equal in diameter. Twice the product of the measurements on the films divided by the sum of the two equals the calculated diameter of the skull. The diameter of the ball divided by the horizontal diameter of its shadow equals the diameter of the skull divided by the calculated diameter of its shadow. A nomogram is used for rapid calculation.—*Eugene J. McDonald, M.D.*

THIERSTEIN, SAMUEL T. Midpelvis diameters. *Am. J. Obst. & Gynec.*, June, 1952, *63*, 1282–1289.

This discussion deals with the manual measurements of 600 consecutive private patients with special emphasis given to midpelvic size. The midpelvis is measured in terms of centimeters by a method which is practical to the young physician studying obstetrics. Manual pelvimetry should conform to several requirements: (1) It must be sufficiently simple so that measurements by different individuals are uniform. (2) It should require no elaborate equipment. (3) It should cause the patient a minimum of discomfort. (4) It should screen out the abnormal patient whose pelvis may prove to be the cause of a cephalopelvic disproportion. The midpelvis has four points which are easily accessible and distances between these points may be measured directly. These points are the apex of the pubic arch, the two ischial spines, and the lower end of the sacrum.

This series reveals that about 5 per cent of the patients have a midpelvic contraction which may cause a complication if the infant's birth weight is greater than 7 pounds. An additional 5 per cent have a borderline midpelvic contraction which may not accommodate an infant larger than 8 pounds. All patients in this series having a dystocia due to cephalopelvic disproportion were among the 10 per cent who had a decreased midpelvic capacity. Many patients with a midpelvic contraction will deliver normally. Strong labor pains will overcome much dystocia due to disproportion. The routine manual measurements with average diameters are given.—*Eugene J. McDonald, M.D.*

GERSHON-COHEN, J., and HERMEL, M. B. Pelvic pneumoperitoneum; the x-ray appearance of the normal female pelvic organs. *Am. J. Obst. & Gynec.*, July, 1952, *64*, 184–187.

The authors took the opportunity of studying the normal pelvic organs in a group of 300 women with pulmonary tuberculosis who had pneumoperitoneum for therapy.

The technique of the examination and the appearance of the normal pelvic organs are described.—*Joseph Levitin, M.D.*

JEFFCOATE, T. N. A. A case of diphallus in the female. *J. Obst. & Gynaec. Brit. Emp.*, June, 1952, *59*, 406–407.

Diphallus is an interesting malformation which occurs in either sex but is more obvious, and is recorded more frequently, in the male.

In the case described here the patient was a seven year old girl who was operated on for a large ventral hernia when she was four years of age, and a little later had one sternomastoid muscle divided for torticollis.

The unusual appearance of the vulva had attracted attention; she had no symptoms except partial incontinence of urine, the significance of this being difficult to assess because of her youth. The labia majora diverged in front and the mons veneris was absent, but it is difficult to be sure how much of this deformity is a result of the previous operation for hernia. The labia minora, with their foreparts well developed for a child of seven years, were quite separate in front, each curling round a clitoris (or half a clitoris). The urethra looked normal but it was probably affected by a minor degree of epispadias.

The paucity of symptoms led to a decision not to undertake any immediate treatment, and it seemed unjustifiable to administer an anesthetic merely to determine more exactly the state of the urethra and the vagina and uterus. A roentgenographic examination, however, revealed a typical "split" pelvis.—*Eugene J. McDonald, M.D.*

DI PALMA, SALVATORE, and BERANBAUM, S. L. The roentgenographic diagnosis of endometritis hyperplastica ovarialis. *Am. J. Obst. & Gynec.*, July, 1952, *64*, 162–167.

This condition is an endocrine disorder characterized by abnormal ovum maturation, and by hyperestrinism due to multiple folliculation and ab-

normal corpus luteum formation. Clinically, it is characterized by prolonged uterine bleeding.

Pathologically there is a marked thickening of the endometrium which has a fungoid or polypoid appearance. It can be treated by irradiation in small doses (80 r to each ovary).

The authors cite 1 case in which a salpingography was done showing what they consider a characteristic roentgen picture, *vis.*, multiple small irregular excavations throughout the entire area of the uterine cavity.—*Joseph Levitin, M.D.*

Messelt, Olaf T. Primary carcinoma of the vagina. *Surg., Gynec. & Obst.*, July, 1952, *95*, 51–58.

Observations are reported upon 78 patients treated in The Norwegian Radium Hospital for primary vaginal carcinoma during the years 1932 to 1945.

1. There were 73 cases of squamous cell and 5 cases of adenocarcinoma.

2. Primary vaginal carcinoma comprised 2.6 per cent of all cancers of the female genital organs treated in The Norwegian Radium Hospital. In proportion to the number of women of twenty-five years or more in the entire country, this gives a ratio of 1 case of primary vaginal cancer to every 160,000 persons in the population.

3. The average age was fifty-six years, with the majority of the patients in the age group between fifty and a sixty-five years.

4. The ratio of married to unmarried women having primary vaginal cancer was 3.9:1, while the ratio of married to single women in the entire country was 0.7:1. Fifty-nine of the 78 patients had had children.

5. Cancer was present among the parents, grandparents, brother, and sisters of 13 patients; there was no history of cancer among the relatives of 56 patients, and no information upon this point for 9 patients.

6. Bleeding was present in 80 per cent of cases. The duration of symptoms, in more than half of the cases, was three months or less. The duration of symptoms was approximately the same in those patients in whom the tumor was clinically "restricted" to the vagina as in the women exhibiting extension to adjacent regions and metastases to lymph nodes.

7. In 65 per cent of cases, the tumor was localized to the posterior wall, and in 66 instances the upper third of the vagina was involved in the process.

8. In 13 cases the inguinal lymph nodes were involved, although there were no clinical indications that the vulva was invaded.

9. Therapy was individualized. The commonest forms of treatment were radium and roentgen therapy. No person was refused treatment. There was a five year cure rate of 22.7 per cent. Age, site of tumor, and therapeutic methods are reviewed in detail for the patients who lived five years or longer. —*Mary Frances Vastine, M.D.*

Genitourinary System

Rosh, Rieva, and Strax, Philip. Intravenous pyelography as an aid in classification of carcinoma of the cervix. *Radiology*, July, 1952, *59*, 107–110.

Carcinoma of the cervix is rarely the immediate cause of death per se. In about 40 per cent of the cases death is due to invasion or obstruction of the urinary tract. Regardless of the clinical stage of the disease, a pathological condition of the bladder, ureters or kidneys is of grave prognostic significance. For this reason, intravenous urography should be done in every case of carcinoma of the cervix before treatment. It often is desirable to repeat these studies during the period when radiation is being administered and on subsequent re-examinations.

Discovery of definite involvement of the urinary tract, such as bladder invasion, ureteral blocking with hydronephrosis, or a nonfunctioning kidney requires reclassification. A case that was classed as Stage II or III may have to be transferred to Stage IV group.

In the period from 1937 to 1946 a total of 638 cases of carcinoma of the cervix were seen in the Radiation Department of Bellevue Hospital. Of these, 371 were classed as Stage IV carcinoma. Forty per cent of this number (148 cases) were originally classed as Stage II or III but had to be transferred to the Stage IV group following urinary tract investigation. Four illustrative cases are reported.—*Arno W. Sommer, M.D.*

Waldron, Edward A. Urethrocystography. *J. Faculty of Radiologists*, July, 1952, *4*, 54–63.

Waldron undertook the investigation of a series of genitourinary patients by urethrocystography in order to determine the indications for this type of examination, the practicability of routine complete urethrocystography in a busy department, and the type of lesions which can be demonstrated.

According to the author, the instrument used consists of a 3 inch curved stainless steel or perspex support, to one end of which is attached a clamp. At the other end are two studs to which is attached an adjustable 1 inch wide rubber band, to clasp the penis. The clamp supports a cannula, the penile end of which carries a rubber Montague lymph ejector. The proximal end of the cannula carries a tap and this takes a normal syringe fitting. For roentgenographic exposures during injection a 6 foot length of rubber tubing is interposed between the cannula and the syringe. This allows the operator to stay at a considerable distance from the roentgen

tube. The contrast medium is 35 per cent pyelosil. To fill the bladder, this is diluted 1 to 6, and 240 to 300 cc. is used. For urethral examination the contrast medium is diluted 1 in 3 and 45 to 60 cc. is used. In deciding what strength of contrast medium was to be used, the quality sought was a strength dense enough clearly to outline the urethra, but not too dense to conceal a diverticulum seen en face nor to conceal a density change due to a condition such as a neoplasm of the bladder wall. The average exposure time is 3/10 second. Three roentgenograms are made *during* the injection, two *during* voiding and one after voiding is complete. Projections during the injection include (a) right posterior oblique, tube vertical, (b) anteroposterior, tube angled 15° toward the head and (c) left posterior oblique, tube angled 15° toward the feet. Projections during voiding are (a) left posterior oblique, tube angled 15° toward the feet and (b) right posterior oblique, tube vertical.

Various conditions discussed and the roentgen appearance described include strictures of the urethra, diverticula of the bladder, residual condition of the prostatic urethra after surgical intervention, urethral diverticulum, prostatic hypertrophy, prostatic carcinoma, prostatic calculi, rectovesical fistula and penile amputation.

Urethrocystography is considered diagnostic in strictures of the bladder, diverticula of the bladder post-prostatectomy states and diverticula of the urethra. Contraindications to this type of examination comprise recent instrumentation, bleeding from the lower urinary tract and acute local infection.

The author concludes that urethrocystography can be readily carried out in a busy department. Routine examinations undertaken by a team familiar with the procedure can be completed in under thirty minutes.—*Samuel G. Henderson, M.D.*

CASTRO, ENRIQUE PÉREZ, and YANGUAS, JUAN DÍEZ. Uréter retrocaval. (Retrocaval ureter.) *Arch. españ. urol.*, 1952, *8*, 183–198.

A case of retrocaval ureter in a thirty-two year old male is presented. For two years the patient had experienced left lumbocostal pain which radiated forward and downward. Left retrograde pyelography revealed a well filled but slightly rotated renal pelvis. The left ureter described an arcuate course, convecity downward, toward the fourth lumbar vertebra, then descended perpendicularly to the bladder. Right retrograde pyelography revealed poor filling of the inferior calyces. The ureter formed an abrupt curve, overlapping the fourth lumbar vertebra, then curved less abruptly back toward a normal course. There was no dilatation of the ureter and renal pelvis above the abnormal curve. Preoperative diagnosis was right retrocaval ureter and left nephrotosis with anomalous vessel at the inferior renal pole. At operation a venous vessel was found anterior to the right ureter, coursing toward the inferior vena cava. This vessel was ligated and severed. A second operation on the left revealed anomalous vein and artery at the inferior renal pole. These were also sectioned. The patient made an uneventful recovery.

Concerning embryology, cardinal and supracardinal veins are present on each side in the fetus. These are usually obliterated, with the exception of the right supracardinal vein, which becomes the vena cava. Persistence of these various venous channels leads to various anatomical states in the adult.—*Charles M. Nice, M.D.*

FINEMAN, SOL, FERBER, WILLIAM L., and ROGINSKY, DAVID N. Primary pneumaturia, with a report of two cases. *Radiology*, July, 1952, *59*, 63–69.

Pneumaturia signifies the passage of gas from the bladder during micturition or on catheterization. Secondary pneumaturia is not uncommon and results from introduction of air or gas into the bladder by instrumentation or through a fistulous opening from a hollow viscus. Primary pneumaturia is rare and is due to fermentation of urine in the bladder through the agency of some fermenting organism. Only 36 cases have been reported in the literature to date, 18 of which were associated with glycosuria and 18 without. Of this total, only 4 had been diagnosed roentgenographically.

The authors report 2 cases that represent the fifth and sixth in which the diagnosis was established or confirmed roentgenographically. Both of these cases were diabetics and presented a diabetic neuropathy with a consequent "neurogenic bladder" which accounted for the residual urine. In other cases the retention was caused by vesical neck obstruction. The exact mechanism of the production of gas is not known but it is believed that in diabetics the glucose in the urine is fermented by bacteria which have exceptional gas-producing properties. This gas must be insoluble in the urine to be detected. In nondiabetics it is thought that the gas is produced through the action of certain bacteria on an albuminous protein present in the urine. The bacteria found in most of the cases reported in the literature were *E. coli*, although *B. aerogenes capsulatus* and *B. lactis aerogenes* have also been found.

Clinically a suprapubic tympanitic mass may be found. Gas is passed at the end of voiding although the patient may not be aware of this. Cystoscopially there will be an explosive passage of gas after the bladder has been emptied of the retained urine, and the bladder mucosa will present varying degrees of inflammation. Roentgenographically a rounded or pyriform gas shadow in the suprapubic region which does not resemble gas in a distanded rectosigmoid may be seen. When an excretory urogram is obtained there will be an opaque medium-urine mixture capped by a large amount of gas in the distended

bladder. With an upright film a fluid level can be demonstrated.

Treatment includes the use of antibiotics, diabetic control and elimination of residual urine by transurethral resection of a small amount of tissue from the posterior margin of the vesical neck. Judicious treatment can eliminate most cases of primary pneumaturia; however, many will succumb as a result of renal insufficiency due to pylonephritis.—*Donald N. Dysart, M.D.*

Engel, William J. Urinary calculi associated with nephrocalcinosis. *J. Urol.*, July, 1952, *68*, 105–116.

This article is a clinical study of 12 patients with nephrocalcinosis diagnosed by roentgen examination. The author dicusses the etiology of the disease and correlates the pathological findings which have been reported elsewhere with the ideas regarding the etiology of primary renal calculi propounded by Randall and later by Keyser.

All but 2 of the 12 cases reported in this article formed stones. In many instances the renal colic produced by these stones called attention to the nephrocalcinosis which was found on roentgen studies. The author theorizes that the primary trouble is renal tubular damage brought on by some nephrotoxic agent, either bacterial or chemical. The calcification follows the tissue damage and occurs chiefly in the distal and collecting tubules and the extratubular tissue of the renal papilla. The tubular dysfunction may give rise to metabolic disturbances, changes in the acid base ratio and disturbances in the calcium and phosphorus metabolism. Stunted growth and rickets have been observed in some instances as a result of the disturbances in calcium metabolism. It is noted that the nephrocalcinosis is not always a diffuse disease, but it may occur in a unilateral or localized portion of a kidney. Furthermore, cases of nephrocalcinosis are known to have existed in which the lesion was not demonstrated by roentgen methods. One might assume that minimal or limited renal tubular damage followed by calcification with extrusion of the calcific deposit, which works it way through the collecting tubules and finally emerges at the tip of the renal papilla, later becoming a nidus for accumulation of the urinary salts, is a reasonable correlation of the Randall theory.

The author believes that as we learn the causes of renal tubular injury, we may also learn the manner in which to prevent many of these primary renal calculi.—*George W. Chamberlin, M.D.*

Miller, Ashton, and Mitchell, J. P. Hyperparathyroidism and renal calculi. *Brit. J. Urol.*, June, 1952, *24*, 91–98.

A single case of bilateral renal calculi due to hyperparathyroidism is reported. The case is unique because the diagnosis was made early before any operations for renal lithiasis were performed.

A complete and concise review of similar cases is given, with a discussion of the incidence of associated renal calculi and hyperparathyroidism, as well as a summary of the clinical characteristics of these conditions. The roentgenologic features are mentioned. —*W. J. Canada, M.D.*

Glaser, S. Simple renal cysts. *Brit. J. Surg.*, July, 1952, *40*, 74–78.

Five cases of simple renal cyst formation are presented with a brief discussion of theories of etiology, incidence, pathology, clinical features, diagnosis and treatment.

The main clinical symptoms are due either to pressure effects in the kidney or on surrounding tissues, or to the presence of a lump. Hematuria is rare. Urography is the most important single method of investigation but is not necessarily diagnostic. The deformities of the calyces and the kidney pelvis encountered in a simple renal cyst or tumor may be similar. Surgical exposure of the lesion is the only reliable method of diagnosis. Hemorrhagic cysts occur and a significant percentage of them have been malignant.

In simple renal cyst, the author recommends excision of the cyst wall to the level of the kidney and destruction of the remainder of the cyst lining by diathermy or chemicals such as Zenker's solution or phenol. Nephrectomy is recommended for hemorrhagic cysts.—*James F Martin, M.D.*

Nichols, Frederick L., Root, Sophie A., Mirabile, Charles S., and Lampson, R. Starr. Cushing's syndrome treated by removal of adrenal-cortex tumor. *New England J. Med.*, July 3, 1952, *247*, 11–15.

Cushing's syndrome is a definite clinical entity; however, it may result from several different causes. Overproduction of adrenal cortical hormones leads to effects on sexuality, electrolytes, and carbohydrate metabolism. In the classical cases either basophilic pituitary tumors or increase in basophilic cells in the anterior pituitary are thought to produce increased amount of ACTH, with resulting adrenal cortical hyperfunction.

The syndrome may be primary in the adrenal cortex due to either tumor or hyperplasia.

The authors present the detailed history of a patient with Cushing's syndrome which subsequently proved to be due to a large carcinoma of the adrenal, practically completely replacing the gland. This large tumor was removed through a transthoracic approach which the authors find distinctly advantageous. Doses of aqueous extract of whole adrenal cortex prevented symptoms of adrenal insufficiency. Several photographs show the excellent

response to surgery up to twenty-six months after operation.

The patient initially presented signs and symptoms of hirsutism, amenorrhea, loss of scalp hair, atrophy of the breasts, loss of fat over the hips, deepening of the voice, and hypertension.

Roentgenographic examination demonstrated osteoporosis, fractured vertebrae, fractured ribs and a large left suprarenal mass compatible with an adrenal cortex tumor. Laboratory studies showed elevated serum sodium, increased 17-ketosteroid excretion, and prolonged drop in the blood sugar curve after tolerance test.

This patient showed remarkable amelioration of symptoms and signs after the operation, and was able to resume teaching, carrying a full schedule.—*Thomas S. Long, M.D.*

RUSCHE, CARL. Testicular tumors: clinical data on 131 cases. *J. Urol.*, July, 1952, *68*, 340–353

An analysis of 131 cases of testicular tumors is presented. These cases were collected from the records of eight hospitals within the Los Angeles area during the six year period from 1942 to 1948.

The classification of Moore and Friedman was used. Embryonal carcinoma and seminoma each comprised 31 per cent of the total tumors, adult teratoma 15 per cent, teratocarcinoma 14 per cent, benign tumors 7 per cent, chorionepithelioma 2 per cent.

There was no significant difference in the mean age of patients afflicted with the various malignant tumors, the mean age for all cases being thirty-six years.

Cryptorchidism did not appear to be a significant factor in predisposing to malignancy. Fifteen of the 131 patients had a unilaterally undescended gonad; 11 of these developed a tumor in the undescended gonad and 4 in the normal gonad. Of a total of 107 undescended testicles removed during the period 1942–1948, in patients whose mean age was thirty-two years, none was found to contain a malignant tumor.

There are no discernible pathognomonic symptoms of testicular tumors. The most common symptom is painless enlargement of the testicle occurring in 98 cases of this series, and painful enlargement occurring in 27 cases. The duration of symptoms and the rapidity of tumor growth are of no value in classification or diagnosis. Trauma is not a component in the genesis of neoplastic growth.

Biopsy for differential diagnosis is condemned and orchiectomy and microscopic examination of the removed tissue is advised.

Metastases occur by way of lymphatics and blood stream. There was a significant relationship between the type of tumor and the incidence of metastases at the time of diagnosis; 15 per cent of the seminomas, 26 per cent of the embryonal carcinomas, 35 per cent of the adult teratomas, 42 per cent of the teratocarcinomas, and 100 per cent of the chorionepitheliomas showed presence of metastases at the time of diagnosis.

Tests for gonadotropic hormone in the urine were found to have no diagnostic significance since a negative test does not rule out the presence of a testicular tumor.

All patients reported were treated by simple orchiectomy, 37 by orchiectomy alone. Seven of these had benign tumors. One patient had preoperative irradiation followed by orchiectomy, 4 pre- and postoperative irradiation, and 88 patients had postoperative irradiation. The total dose varied from 3,000 r to 34,000 r in the various tumors. Survival within each tumor group was not found to be related to amount of radiation. The mortality rate was highest during the first two years following diagnosis and fell to zero after a four year survival.

The author condemns preoperative irradiation of testicular tumors because: 1. Valuable time is lost before the tumor is removed. 2. Irradiation destroys the original architecture of the tumor complicating microscopic diagnosis. 3. Benign tumors inadvertently are irradiated. 4. Some tumors are radiosensitive and others are radioresistant.

The therapeutic value of irradiation was demonstrated in seminoma, requiring a tumor dose of 1,500–2,000 r, and in embryonal carcinoma and teratocarcinoma, requiring a tumor dose of 5,000–7,000 r. The adult type teratoma is radioresistant; chorionepithelioma likewise is radioresistant and spreads so early through veins that irradiation is useless. The only hope of improving results lies in earlier diagnosis.—*George W. Chamberlin, M.D.*

NERVOUS SYSTEM

PAILLAS, J. E., VIGOUROUX, R., VIGOUROUX, M., and ROGER, A. L'épilepsie en foyer de l'enfant; étude clinique, électrographique et thérapeutique de 234 observations. (Focal epilepsy of the child; clinical, electrographic and therapeutic study of 234 observations.) *Rev. neurol.*, 1952, *86*, 300–318.

Epilepsy of the child is essentially an evolutive epilepsy, partly due to its cause (infectious, traumatic, or degenerative), and partly due to the progressive maturation of the nervous system explaining the different responses that the brain furnishes to the same excitation.

Concerning etiology, 72 cases of 234 were of unknown origin (30.9 per cent). Prenatal causes were present in 14 cases, or 5.9 per cent. These included malformation (dysgenesias and dysplasias) in 6 cases: multiple dysgenesias (syndactylia, absence of finger), 2 patients with Sturge-Weber-Krabbe disease. In 8 cases encephalic lesions of toxic, infectious or parasitic origin apparently started *in utero:* 2

cases of hereditary alcoholism, 2 of syphilitic encephalitis, 1 of toxoplasmosis and 3 of grave encephalopathy of uncertain nature. Natal causes were present in 71 cases, or 30.3 per cent. These included birth trauma due to forceps in 35 and various dystocias in 36. Postnatal causes were present in 77 cases, or 32.9 per cent. These included trauma in 24 cases, infectious diseases of childhood in 51 cases, and 2 cases of malaria. Two-thirds of the cases presented signs of unilateral or bilateral cerebral atrophy.

Sixteen cases were operated upon and furnished data of interesting anatomic alterations. In the case of the patient with Sturge-Weber-Krabbe disease an area of sclerotic tissue invading the white matter of the occipital lobe, dilated pial vessels, cellular infiltration of vascular walls and calcaneous deposits in the middle and deep cortical layers were seen. Utilizing Penfield's classification, the other 15 cases were tabulated. There were 2 cases of meningocerebral cicatrix, 5 cases of localized cortical atrophy, 1 of serous cyst, 2 of subcortical cicatrix, 4 of localized arachnoiditis, and in 1 case no macroscopic change was noted even though there was focal electroencephalographic change.

Pneumography often permits follow-up of the evolution of cerebral cicatrices. Thus, accentuation of ventricular dilatation, enlarging deformation of one horn, or enlargement of a porencephaly testify to the aggravation of retactile atrophic process.

Clinical neurologic examination is of great importance. Nature of crises and associated neuropsychiatric symptoms and evolutionary changes are likewise important. Electroencephalographic studies may be of aid.

In 32 patients who had roentgenographic studies five types of anomalies were revealed: (1) 14 presented abnormally accentuated cerebriform impressions; (2) diffuse deformation in the form of microcephaly (2 cases) or augmentation of cranial volume with protrusion of the temporal fossae were noted; (3) cranial hemiatrophy was seen in 8 patients; (4) calcifications were found in toxoplasmosis and Sturge-Weber-Krabbe disease; (5) lacunar skull was observed in 2 cases of posttraumatic epilepsy.

Sixteen of 24 patients undergoing pneumography revealed different types of anomalies. Anomalies of the ventricles included retraction of the third ventricle in 3 cases. Three of 16 had generalized ventricular enlargement, while in 13 the enlargement was unilateral or involved a single horn. Distention of subarachnoid spaces, especially frontoparietal and insular, and meningeal symphysis, marked by absence of air in localized portions of the convexity, were also noted.

Of the 16 patients treated surgically, 11 were evaluated at least one year after operation. Four children have not had a crisis, 1 had 75 per cent amelioration and 4 had 25–50 per cent amelioration.—*Charles Nice, M.D.*

Goinard, Pierre, and Descuns, Pierre. Les kystes hydatiques du névraxe. (Hydatid cysts of the nervous system.) *Rev. neurol.*, 1952, *86*, 486–488.

This is a short discussion concerning the subject. It is pointed out that huge hydatid cysts in children will cause enormous deformation of the cranium with considerable separation of the sutures. In spite of this wide separation of the sutures, there is always papillary edema.

The importance of arteriography is stressed in the localization and pathological diagnosis of hydatid cysts of the nervous system, based on the displacement of the vascular system and the absence of vascularization of the lesion itself. Toxoplasmosis and meningioma should be differentiated from intracranial hydatid cysts. Arteriography is of definite help in differentiating meningiomas because of their rich vascularization.—*Jirair N. Sarian, M.D.*

Skeletal System

Erlacher, Peter R. Nucleography. *J. Bone & Joint Surg.*, May, 1952, *34-B*, 204–210.

In this paper, a technique of nucleography, in which a radiopaque solution of iodine is injected into the nucleus pulposus for contrast roentgenography, is described. Experimental work demonstrated that the following five principal disc forms occurred although not all were true to type: Form 1, the globular nucleus, found mostly in young subjects, denoting a healthy disc without degeneration or herniation; Form 2, the lobed nucleus, the usual form in adults, showing a few large lobulations with unlikely occurrence of degeneration or herniation; Form 3, the simple branched nucleus, showing a central shadow with a few long and narrow branches, which predisposes to herniation; Form 4, the multiple branched nucleus, having a small central shadow and several branches in various directions, which is a transitory form of degeneration in which prolapse is likely to occur; Form 5, the spread nucleus, showing multiple branches in all directions instead of the central shadow. This form represents the typical degenerated disc and is most likely associated with narrowing of the disc, in which herniation must no longer be expected.

The author thinks the most important forms for clinical diagnosis are the simple branched nucleus (Form 3) and the spread nucleus (Form 5).

The various forms are illustrated by line drawings and the roentgenographic technique is described in full. The contrast medium used is marketed under the trade name "joduron" by Cilag, Schaffhausen, Switzerland. The position of the injecting needle is checked by anteroposterior and lateral roentgenograms. The films must be made quickly after injection because the medium diffuses rapidly. The

following views are recommended: anteroposterior lateral, right and left obliques with the patient turned at an angle of 15 degrees.

The author believes that with this technique it should be possible under normal conditions to remain outside the coverings of the spinal cord. The puncture as he describes it, causes little disturbance to the patient. Undesirable sequelae such as are found after injection of oily iodine solutions into the spinal theca need not be feared. Material taken from postmortem specimens has shown that after as little as four hours the solution has diffused to such extent that it is no longer visible in roentgenograms. In life, absorption is added to diffusion and the fluid injected at nucleography will disappear completely in a few hours. The iodine is absorbed from the theca and excreted by the kidney, so that the renal pelvis may be seen in roentgenograms. Because of this rapid excretion iodine disturbances do not occur.

The author suggests that myelography and nucleography both have a place. Myelography enables a general examination of the affected area, whereas nucleography allows a more accurate interpretation of changes found in a particular disc by previous myelography. It is possible to show by nucleography the shape of the herniation which, because of its lateral position or its small size, may not be shown in the myelogram.—*Ralph S. Bromer, M.D.*

KORNBLUM, DANIEL, CLAYTON, MACK L., and NASH, HENRY H. Nontraumatic cervical dislocations in rheumatoid spondylitis. *J.A.M.A.*, May 31, 1952, *149*, 431–435.

The occurrence of dislocations in peripheral joints affected with rheumatoid arthritis is well known, but it is not generally realized that cervical spine subluxations may likewise complicate rheumatoid spondylitis. Stammers and Frazer and Rand have reported cases of spontaneous subluxation of the atlas in patients with rheumatoid spondylitis. The authors present 4 cases which show that lower cervical as well as atlanto-axial dislocations may occur in cervical spondylitis and they feel that early recognition and treatment of these complications are important.

The etiological factors involved in spontaneous cervical dislocations have been discussed in the literature mainly as related to the atlanto-axial joint. It is probable that the same pathological process occurs in other cervical articulations. The squence of events is as follows: (1) cervical infection with hyperemia; (2) vertebral decalcification and loosening of ligamentous attachments; and (3) forward slipping of one or both lateral articular facets of the atlas. Hyperemia, capsular distention and ligamentous relaxation occur in active rheumatoid arthritis and seem to explain why the dislocations take place during the active phase of the disease. The dislocation in most cases develops slowly and occurs without clinical evidence of spinal cord compression.

The roentgenological evidence of atlanto-axial dislocation is quite definite. In the lateral view there is an abnormal forward position of the anterior arch of the atlas in relation to the odontoid. Normally the interval between this arch and the odontoid should not be more than 1 to 2 mm. In the lateral view also there may be an abnormal inclination of the atlas, so that its posterior arch is brought away from that of the axis closer to the occiput. The obliteration of the atlanto-axial joint space in the anteroposterior projection is considered to be the lateral mass of the atlas overlapping the articular facet of the axis.

Dislocations below the atlanto-axial joint generally show obvious malalignment of the cervical bodies. The subluxation of the corresponding articulations and deossification in the articular facets are clearly visualized.

Methods of treatment include manipulation under anesthesia, fixation in a plaster jacket, and head traction with sling or tongs. The last mentioned method was used in 3 of the authors' 4 cases.—*Arthur B. Smith, M.D.*

THOMAS, DAVID F. Vertebral osteoarthropathy or Charcot's disease of the spine; review of the literature and a report of two cases. *J. Bone & Joint Surg.*, May, 1952, *34-B*, 248–255.

Vertebral osteoarthropathy occurs most commonly in the fifth and sixth decades. In many of the reports in the literature, there is a description of the clinical evidence of tabes dorsalis and in others the presence of such evidence is explicitly mentioned. The serological tests are not always positive. The common site is the lumbar region, especially the second, third, fourth and fifth vertebrae. The lower thoracic spine is sometimes involved, either alone or in association with the lumbar segments. The chief roentgenographic features are gross disorganization and destruction together with massive new bone formation. The new bone formation occurs either as very large beaked osteophytes or as massive paravertebral deposits. The formation of new bone may lead to ankylosis. The disc spaces are narrowed. The transverse processes are sometimes involved in the destructive and proliferative process. Sclerosis of the bone end beneath the articular cortex has been mentioned in the literature as an important sign.

Trauma may be a factor in determining the development of spinal osteoarthropathy in a tabetic subject. Vertebral osteoarthopathy must be differentiated from an old traumatic condition such as for instance, Kümmell's disease. Tuberculous disease does not show the new bone formation or sclerosis and it is associated with pain and restriction of movement.

Antisyphilitic treatment is of no avail in controlling the progress of neuropathic joints. Spinal fusion may be justifiable in spinal osteoarthropathy. Support by a suitable corset is regarded by the author as probably the best measure and was used in 2 of his cases with good effect.—*Ralph S. Bromer, M.D.*

Craig, Winchell McK., Svien, Hendrik J., Dodge, Henry W., Jr., and Camp, John D. Intraspinal lesions masquerading as protruded lumbar intervertebral disks. *J.A.M.A.*, May 17, 1952, *149*, 250–253.

From a study of 1,296 cases in which operation was performed at the Mayo Clinic for intraspinal lesions at or below the level of the 10th thoracic vertebra, it is evident that the symptoms and signs of spinal cord tumors that originate at the level of the 10th thoracic vertebra or lower may simulate those of the protruded lumbar intervertebral disc. In these instances, the true nature of the lesion producing the signs and symptoms cannot be determined from the history, and neurological, orthopedic or simple roentgenographic examination. However, when intraspinal investigation consisting of analysis of spinal fluid and contrast myelographic studies is carried out, the presence of intraspinal tumor becomes evident and its location is established in most instances. In those cases in which intraspinal investigation does not establish the true nature of the lesion, myelographic study with a contrast medium does localized the lesion accurately. In this way the surgeon can be directed to the site of the lesion and the proper diagnosis can be established at operation. By analysis of spinal fluid and contrast myelographic studies, a significant number of errors can be avoided. —*James J. McCort, M.D.*

Miyakawa, George. Congenital absence of the odontoid process; a case report. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 676–677.

A case of congenital absence of the odontoid process is reported. The patient was a twenty-nine year old white man who gave a history of injury to the neck at the age of sixteen as a result of wrestling. The injury was sustained by a sudden twisting motion. He was asymptomatic for a period of three years at which time while tumbling he again sustained a sudden jarring motion at the base of the spine. A third injury occurred as the result of striking his head on a large wooden beam, which produced temporary paralysis of both arms together with uncontrolled, uncoordinated movement of the arms. He also had a recurrence of tingling, hyperesthesia and paresthesia, such as had occurred in the previous injuries.

The roentgen examination showed an absence of the odontoid process, an uncommon congenital anomaly. In the differential diagnosis, the possibility of early childhood fracture with atrophy must be considered.

The patient, who is a physician, is leading at the present a normal life. There is, however, the danger of recurrence with possible permanent damage. The author feels that surgical fixation is desirable.—*Ralph S. Bromer, M.D.*

McLaughlin, Harrison L. Posterior dislocation of the shoulder. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 584–590.

Posterior dislocation or subluxation of the shoulder is sufficiently uncommon so that the lesion is often not recognized. Clinical and roentgenographic evidence of the condition is always present. The signs and symptoms are constant and unequivocal although the signs may be missed unless sought for. They consist of a decreased palpable anterior prominence of the humeral head, an increased palpable prominence of the coracoid, increased prominence of the humeral head below the acromion, marked limitation of abduction, and a complete absence of external rotation.

According to the author, roentgen examination by films exposed in anteroposterior projection was difficult and at times impossible. The absence of abduction prevented satisfactory roentgenograms through the axilla, and transthoracic exposures were unsatisfactory. He recommends an exposure made with the patient erect and facing the cassette obliquely, so that the central ray corresponds to the long axis of the spine of the scapula. Such a technique caused no additional damage or discomfort to the patient and proved or disproved the diagnosis with certainty.

Recent posterior dislocations, recognized and treated at once, responded rapidly and well to simple measures. Recurrent or unreduced posterior dislocations required operative treatment. The author states that some failures of surgical treatment for habitual anterior dislocations of the humeral head result from the fact that the recurrent episodes were in reality posterior subluxations of the humerus.—*Ralph S. Bromer, M.D.*

Knight, Robert A., and Van Zandt, I. L. Arthroplasty of the elbow; an end-result study. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 610–617.

This article is an evaluation of the results in 45 of 93 patients on whom arthroplasty of the elbow had been performed, between 1921 to 1948. The conditions causing the ankylosis of the joint were atrophic arthritis, infective arthritis, closed fractures and fracture-dislocations, open fractures and fracture-dislocations and osteochondromatosis. The contraindications for arthroplasty are: (1) those cases in which the patient requires a strong, stable extremity for hard physical labor, that is, if strength

and stability are more important than motion; (2) tuberculosis; (3) osteomyelitis, either hematogenous or associated with open fractures; (4) extra-articular ankylosis, such as may follow an infected open supracondylar fracture of the humerous with antecubital scarring and capsular contracture; and (5) marked muscular weakness, particularly of the biceps and forearm muscles. This latter condition is usually the end result of long-continued inactivity, such as is found in advanced cases of atrophic arthritis.

The technique of operation, after-care, and complications are discussed in the article.

In their conclusion, the authors state that 56 per cent secured good results, 22 per cent fair results and 22 per cent obtained unsatisfactory results. The roentgenographic findings in most instances failed to give a true picture of clinical function. The functional and roentgenographic results, with few exceptions, showed little change after the first year following operation. They believe that fascial arthroplasty of the elbow, properly performed in selected cases, offers a reasonable expectation of 70 to 120 degrees of motion in a useful range, with good strength and stability, and with little if any pain except after strenuous use.

Roentgenograms are shown illustrating preoperative appearances and end results.—*Ralph S. Bromer, M.D.*

PHALEN, GEORGE S. Calcification adjacent to the pisiform bone. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 579–583.

Two cases of calcified pisiform bursitis are reported in this paper. The characteristic symptoms of the condition are pain and weakness of grip, the pain being located over the pisiform. The calcific deposit is adjacent to the pisiform bone and is located either within the tendon of the flexor carpi ulnaris or within the bursa of the flexor carp ulnaris muscle.

The diagnosis is frequently missed because the calcification is usually demonstrated only on oblique roentgenograms of the wrist, with the forearm in mid-supination. This position places the pisiform apart from the other carpal bones and thus the calcification can be demonstrated without overlapping bony shadows. Surgical excision of the calcification is only advised if more conservative treatment fails to give relief. The majority of patients are promptly cured by local infiltration of the calcified area.

Phalen states that anatomically there is no structure which is designated as the pisiform bursa. There is a bursa of the flexor carpi ulnaris muscle, which is situated immediately beneath the tendon of this muscle near its insertion into the pisiform bone. Actually, from a clinical standpoint, it makes little difference whether the calcification is located within the tendon of the flexor carpi ulnaris or within the bursa of the flexor carpi ulnaris muscle. He therefore thinks it best to designate all of these cases of calcification adjacent to the pisiform bone as "calcified pisiform bursitis," the term being descriptive rather than implying a true pathological entity.—*Ralph S. Bromer, M.D.*

HØYER, ANDREAS. Treatment of supracondylar fracture of the humerus by skeletal traction in an abduction splint. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 623–637.

Three methods of treatment of supracondylar fracture of the humerus are in common use: (1) manipulative reduction and fixation in a plaster cast with a "collar-and-cuff" sling; (2) open reduction and fixation; (3) sustained traction. Each method has its warm advocates. Høyer's study of his material indicates that the results of supracondylar fracture of the humerus treated by skeletal traction according to Semb's method are superior to those obtained by treatment with manipulative reduction and plaster. He concludes that only fractures without displacement or those with backward displacement of slight degree should be treated by the application of a plaster cast, or by closed reduction and plaster fixation. In fractures with more extensive displacement, traction or operative treatment seems to be preferable.

The method described consists of the insertion of a small hook-clip through two small skin incisions in the olecranon. The fracture is reduced preferably under the fluoroscope, and the arm is placed on an abduction splint which is illustrated in the paper. The traction is maintained by rubber tubing, and is continued for an average of twenty-one days.

The paper is profusely illustrated with reproductions of roentgenograms, line drawings of the method and tables showing analysis of his cases.—*Ralph S. Bromer, M.D.*

DEPALMA, ANTHONY F. Comminuted fractures of the distal end of the radius treated by ulnar pinning. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 651–662.

It is common knowledge that loss of length of the radius, diminution or obliteration of the radial tilt of the articular surface of the radius, and supination of the distal segment of the radius are the three factors chiefly responsible for poor cosmetic and functional results in cases of fracture of the distal end of the radius. The method of treatment described in this article by DePalma was suggested to him by Henry Briggs. A survey of Colles' fractures by Gartland and Werley demonstrated that two factors govern the final functional capacity of the wrist: complete restoration of anatomical alignment of all fragments and maintenance of this position until healing is complete. The study further disclosed that

plaster fixation for an average period of six weeks does not preclude redisplacement of the fragments.

The method of treatment described consists essentially in reduction of the fracture by traction and molding of the fragments. The corrected position is maintained by means of a threaded wire passing through the ulna to the most distal radial fragment, which invariably includes the styloid process of the radius. The operation is described in detail and some of the pitfalls encountered are mentioned, such as the necessity for use of a threaded wire in all instances, excessive traction which may cause distraction of the fragments and mandatory eight week period of internal fixation. In several cases where the wire was removed at the end of six weeks, shortening of the radius and malalignment of the fragments occurred.

The use of the method in cases where all components of the fracture were corrected has yielded a satisfactory percentage of excellent and good results. No infection occurred when a threaded wire was used and cut below the level of the skin. In 2 cases in which an unthreaded wire was used and the wire was left protruding from the skin, a mild low grade infection developed around the pin site which subsided readily upon removal of the pins.

Reproductions of roentgenograms showing the fractures before and after reduction and the end results are included in the article.—*Ralph S. Bromer, M.D.*

Acheson, Roy M. Radiographs of the hand as an index of skeletal maturity in infants. *Arch. Dis. Childhood*, Aug., 1952, *27*, 382–385.

Using the criterion of failure of ossification of both hamate and capitate at one year of age, 8 out of 561 children demonstrated skeletal immaturity: 6 were boys, 2 were girls. One child was a cretin, previously undiagnosed. Three were light at birth, one of whom was premature with severe physiological jaundice. Only the cretin showed similar retardation of ossification in the knees.

There was little correlation of bone findings with physical or mental development, dentition, closure of fontanelles, I. Q., feedings, social background, or illnesses. Lighter weights at birth and at one year seemed to correlate with bone development in the entire group of 561 children.—*Fay H. Squire, M.D.*

Cleveland, Mather, and Winant, Edward M. Treatment of non-union in compound fractures with infection. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 554–563.

The cases discussed in this paper were not cases of delayed union. They were true ununited fractures. All except one of these were either infected as the result of a compound wound or secondarily following surgery for the original fracture. A method of grafting using multiple chips and ribbons of fresh autogenous cancellous iliac bone was employed. The grafts were placed in abundance about the ununited fracture. Usually no attempt was made to excise the fibrous tissue between the fractured ends of the bone. The cortex proximal and distal to the fracture line was partially removed to promote bleeding and to produce a raw surface. These multiple cancellous grafts resembled a severely comminuted fracture, which usually heals more readily than does the complete cortical fracture without comminution.

Five of the 10 patients of the series are briefly described in the paper. The method of treatment was successful in 9 of 10 difficult cases, in 8 of which infection was present. The cancellous bone grafts from the ilium are advocated because they are rapidly revascularized and are readily incorporated into the host bone. They do not tend to sequestrate in the presence of infection. The authors stress adequate treatment of associated soft tissue wounds and infection. Their procedure has been: (1) to attempt to control infection; (2) to replace devitalized scar with adequate skin; (3) to proceed with bone-grafting.

The paper is illustrated with reproductions of roentgenograms showing the progress in union of several of the cases.—*Ralph S. Bromer, M.D.*

Ferguson, Angella D., and Scott, Roland B. Congenital absence of the tibia; report of a case in a Negro infant. *A.M.A. Am. J. Dis. Child.*, July, 1952, *84*, 84–89.

A case of congenital absence of the tibia in a Negro infant is reported. The theories of the origin of the rare anomaly are discussed in the paper. The roentgenograms of the patient revealed a complete absence of the right tibia and proximal tibial center of ossification.

In these cases, roentgenograms may show complete or partial absence of the tibia. When a portion of the tibia is absent, it is usually the middle or lower part, the proximal portion tapering to a cone. The patella may be absent or situated in an abnormal place. The fibula may articulate with the external condyle of the femur or be displaced backward and up on the shaft of the femur. It may be bent, hyperplastic, defective or normal. Most of the cases of malformation of the tibia are associated with congenital abnormalities in other organs and congenital scars and dimples, which would lead one to suspect defects of bone.

Treatment is controversial and in general unsatisfactory according to the authors, and prognosis for normal locomotion is poor.

The theories of origin which are discussed include (1) heredity, (2) endogenous or germinal origin, (3) fracture or trauma, (4) neuronervous origin, (5) nutrition, (6) amnion adhesions, and (7) virus origin.—*Ralph S. Bromer, M.D.*

Farmer. A. W. The use of a composite pedicle

graft for pseudarthrosis of the tibia. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 591–600.

Three children with pseudarthrosis of the tibia were treated by the author with cutaneous-bone pedicle grafts in order to determine whether such a method would constitute a successful form of therapy for this condition at this age level. Although the principle appeared sound, he does not recommend the operation as described. Union between the graft and the upper tibial fragment occurred rapidly. He thinks that technical difficulties may have been the cause of the delay in fusion at the lower level. It may be possible to overcome some of these difficulties by the use of a bone pedicle graft from another area, such as the ulna. Accurate approximation of the graft to the tibial fragments at the time of the initial transfer might then be possible.

The paper is illustrated with reproductions of roentgenograms showing the union at the upper end of the graft and delayed union at the lower end in several of the cases.—*Ralph S. Bromer, M.D.*

Fonda, Maxwell P. Dislocation of the tibiotalar joint without fracture; an unusual ski injury. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 662–664.

The author found in a review of the literature that a complete dislocation of the ankle joint without an associated fracture is a relatively uncommon injury. In none of the cases cited from his review had the injury resulted during skiing. He thought it also worthy of note that in a very large series of injuries sustained in parachute jumping there was no mention of any case of complete dislocation of the tibiotalar joint without fracture.

The patient stated that his injury occurred when he fell in attempting a turn, locking the left ski over the back of the right one. In this position his foot was in marked plantar flexion and the left knee was partially flexed. On roentgen examination a marked posterior dislocation of the talus on the tibia was shown, with the talus lying slightly lateral and completely posterior to the tibia and fistula. Reduction under spinal anesthesia was accomplished with gentle traction with the knee bent at a 45 degree angle. The end result was excellent, with complete range of motion of the ankle.—*Ralph S. Bromer, M.D.*

Baggenstoss, Archie H., Bickel, William H., and Ward, L. Emerson. Rheumatoid granulomatous nodules as destructive lesions of vertebrae. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 601–609.

In one of the cases reported in this paper, a patient with rheumatoid arthritis, granulomatous nodules were observed clinically in the subcutaneous tissue and at necropsy in the synovial membranes, pericardium, myocardium, subchondral bone and vertebrae. The granulomatous process in the spine caused compression fracture of the twelfth thoracic vertebra and appeared similar, roentgenographically, to such other destructive lesions as multiple myeloma, metastatic carcinoma and tuberculosis.

Three other cases in addition are reported which emphasizes the fact that the granulomatous inflammation which is so commonly observed in the subcutaneous tissues and occasionally in the viscera of patients with rheumatoid arthritis may also involve the vertebrae. This fact is of importance in the consideration of the differential diagnosis of destructive lesions of vertebrae in patients with rheumatoid arthritis.

Even at necropsy, in the first case reported, the gross examination failed to reveal the nature of the process which had caused destruction of the vertebral bodies and the pericarditis. The lesions in the vertebrae were interpreted as myelomatous in character until histopathological examination revealed their true nature.

The paper is illustrated with reproductions of roentgenograms of the vertebrae which were affected and with photomicrographs of the vertebrae and pericardium.—*Ralph S. Bromer, M.D.*

Goldenberg, Raphael R., and Wild, Eugene L. Chondromalacia fabellae. *J. Bone & Joint Surg.*, July, 1952, *34-A*, 688–690.

Degenerative changes of the articular surface of the fabella in the gastrocnemius muscle have been designated chondromalacia fabellae by the authors. Localized tenderness and pain on passive motion of the fabella appear to be the chief diagnostic criteria. The fabella is cancellous in structure and the free surface is covered with smooth articular cartilage. The remaining portion of the bone possesses no periosteum and is invested by the fibrous tissue of the gastrocnemius. On roentgenographic examination, the contour of the fabella appears to be either semilunar or pyramidal in shape in the lateral view and somewhat circular in the anteroposterior view. In the cases reported, there was no evidence of osseous involvement of the fabella.

The cure consists in the removal of the involved fabella. The authors state that if at operation that portion of the posterior articular surface of the lateral condyle of the femur which is in intimate contact with the fabella shows evidence of degenerative change, this portion of the condyle should also be removed.—*Ralph S. Bromer, M.D.*